"Biomedical Engineering Technologies for Skin Aging: From Biosensors to AI-Driven Cosmeceutical Design"

Sanika Shivaji More, Samruddhi Anand Patil, Vaishnavi Bhimrav Patil, Shriya Ranjit Patil, Sahyadri Deelipkumar Ugale, Sonali Krishna Diwate*

Department of Quality Assurance, D. Y. Patil College of Pharmacy, D. Y. Patil Education Society (Deemed To Be University), Kolhapur, Maharashtra, India. 416011

***Corresponding Author**

Email: sonalikd28@gmail.com

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ABSTRACT

Background

Skin aging is a multifactorial biological process influenced by intrinsic factors such as genetics and extrinsic factors including ultraviolet radiation, pollution, and lifestyle. While conventional approaches rely primarily on topical interventions, recent advances in biomedical engineering have introduced novel tools for the analysis, monitoring, and management of skin aging.

Objective

This review aims to examine emerging biomedical engineering technologies—including biosensors, advanced imaging systems, microfluidic models, and artificial intelligence—in the assessment and management of skin aging.

Methods

A comprehensive literature search was conducted using databases such as PubMed, Scopus, and Web of Science, covering publications from 2010 to 2025. Studies focusing on biomedical technologies, skin aging mechanisms, and cosmeceutical development were systematically reviewed and analyzed.

Results

Technologies such as transepidermal water loss (TEWL) sensors, optical imaging systems, and wearable biosensors enable real-time monitoring of skin barrier function and physiological parameters. Microfluidic and organ-on-chip platforms provide advanced in vitro models for studying skin structure and function under controlled conditions. In parallel, artificial intelligence and machine learning approaches facilitate predictive modeling, formulation optimization, and personalized skincare strategies. Collectively, these technologies enhance mechanistic understanding of skin aging and support the development of targeted cosmeceutical interventions.

Conclusion

The integration of biomedical engineering tools with dermatological research presents significant opportunities for precision skincare and anti-aging therapy development. These technologies enable data-driven design, improved evaluation of cosmeceuticals, and the advancement of personalized approaches to skin aging management.

Keywords

Skin aging, biomedical engineering, biosensors, artificial intelligence, cosmeceuticals, TEWL, systems biology

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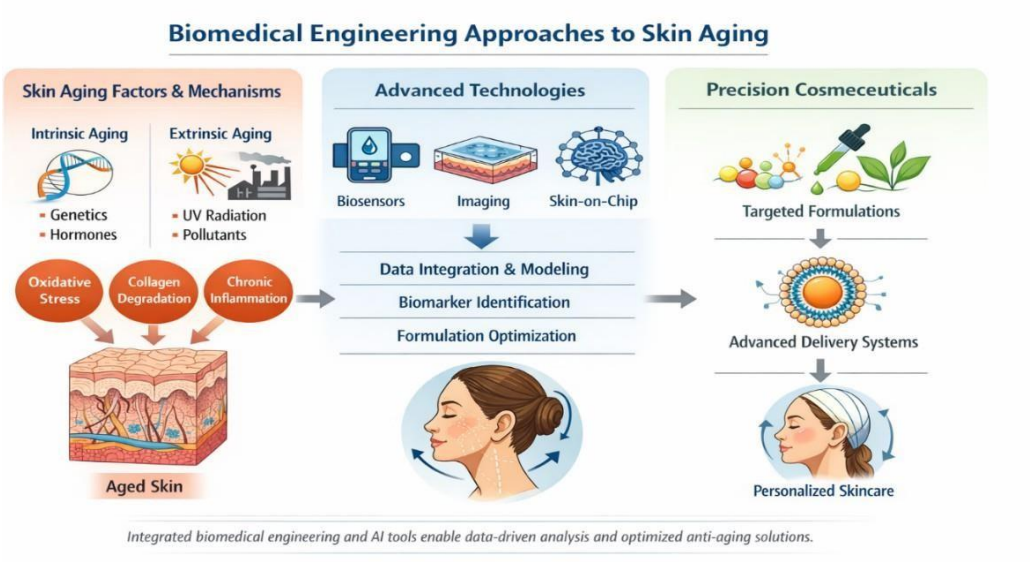
Graphical Abstract

Biomedical engineering technologies are reshaping the understanding and management of skin aging by enabling systems-level analysis and data-driven cosmeceutical design. Both intrinsic and extrinsic aging factors initiate molecular processes such as oxidative stress, collagen degradation, and chronic inflammation, resulting in progressive structural and functional changes in the skin. Advanced tools—including biosensors, high-resolution imaging systems, microfluidic skin-on-chip models, and artificial intelligence—facilitate real-time monitoring, detailed characterization, and predictive modeling of these processes.

Integration of multi-omics data with computational modeling and machine learning further supports the identification of key biomarkers and the rational optimization of formulation strategies. In parallel, engineering-driven approaches such as nanocarrier-based delivery systems and Quality by Design (QbD) frameworks enhance the stability, bioavailability, and targeted delivery of anti-aging compounds, including plant-derived bioactives.

Collectively, this integrated framework enables a shift from conventional skincare approaches toward precision cosmeceuticals, where interventions are tailored to individual skin profiles. The convergence of biomedical engineering, artificial intelligence, and dermatological science thus provides a foundation for personalized, predictive, and preventive strategies in skin aging management.



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INTRODUCTION

Skin aging is a multifactorial biological process characterized by progressive structural and functional changes in the skin over time[101–103]. These changes arise from the combined influence of intrinsic factors, such as genetic predisposition and chronological aging, and extrinsic factors including ultraviolet (UV) radiation, environmental pollution, and lifestyle habits[101,104]. Clinically, aging skin presents as wrinkles, reduced elasticity, dryness, uneven pigmentation, and impaired barrier function, contributing to both aesthetic concerns and dermatological conditions[101,102].

At the molecular level, skin aging is associated with alterations in extracellular matrix composition, increased oxidative stress, mitochondrial dysfunction, and chronic low-grade inflammation [1,5,101]. Degradation of collagen and elastin fibers, primarily mediated by matrix metalloproteinases (MMPs), leads to diminished dermal integrity and elasticity [1,5]. Concurrently, reactive oxygen species (ROS) generated by environmental stressors accelerate cellular damage and disrupt normal physiological processes. These interconnected pathways underscore the complexity of skin aging and highlight the need for advanced analytical and predictive approaches [1].

Traditional dermatological and cosmeceutical strategies have largely focused on topical formulations containing antioxidants, retinoids, peptides, and botanical extracts [22–24]. Although these interventions offer therapeutic benefits, their evaluation has historically relied on subjective assessments or limited biochemical assays. The lack of real-time, quantitative monitoring tools has constrained precise assessment of skin condition and treatment efficacy [101,105].

Recent advances in biomedical engineering have begun to address these limitations by introducing innovative technologies for the assessment, modeling, and management of skin aging [101,105]. Biosensors capable of measuring parameters such as transepidermal water loss (TEWL), hydration, pH, and temperature enable non-invasive, continuous monitoring of skin function. Advanced imaging modalities, including confocal microscopy and optical coherence tomography, provide high-resolution visualization of skin structure and morphology. In parallel, microfluidic platforms and skin-on-chip systems offer controlled environments for studying skin physiology and evaluating therapeutic interventions.

Furthermore, computational approaches—including systems biology, network pharmacology, and artificial intelligence—have emerged as powerful tools for analyzing complex biological datasets and predicting treatment outcomes. These technologies support the rational design of targeted and personalized cosmeceutical formulations through integration of molecular, cellular, and environmental data.

This review provides a comprehensive overview of biomedical engineering technologies applied to skin aging, with a focus on biosensors, imaging systems, microphysiological models, and AI-driven cosmeceutical design. By bridging engineering innovation with dermatological science, it highlights emerging opportunities for precision skincare and advanced anti-aging strategies.

2. Biological Mechanisms of Skin Aging

Skin aging results from the interplay of intrinsic (chronological) and extrinsic (environmental) factors that collectively influence cellular function, structural integrity, and biochemical processes within the skin. A clear understanding of these mechanisms is essential for developing targeted diagnostic and therapeutic strategies.

2.1 Intrinsic Aging

Intrinsic aging, or chronological aging, is a genetically programmed process that occurs naturally over time. It is characterized by gradual physiological changes, including reduced cellular turnover, decreased fibroblast activity, and diminished synthesis of structural proteins such as collagen and elastin [101].

A central feature of intrinsic aging is telomere shortening, which limits cellular replication and promotes cellular senescence. Senescent cells accumulate within the dermis and exhibit a senescence-associated secretory phenotype (SASP), releasing pro-inflammatory cytokines, growth factors, and proteolytic enzymes that contribute to tissue degradation and impaired regeneration [91–93].

Mitochondrial dysfunction further accelerates intrinsic aging. Reduced mitochondrial efficiency leads to decreased ATP production and increased generation of reactive oxygen species (ROS), amplifying oxidative damage [1,5]. In addition, age-related hormonal changes and declining antioxidant defenses exacerbate oxidative stress, further compromising skin homeostasis [1].

2.2 Extrinsic Aging

Extrinsic aging is driven primarily by environmental and lifestyle factors and is often referred to as photoaging when associated with ultraviolet (UV) exposure [1,5,101]. Among these factors, UV radiation is the most significant contributor, inducing direct DNA damage and generating ROS that accelerate cellular aging [101,104].

UV exposure activates signaling pathways that upregulate matrix metalloproteinases (MMPs), leading to degradation of collagen and other extracellular matrix components. This process results in wrinkles, loss of elasticity, and structural disorganization of dermal tissue.

Environmental pollutants, including particulate matter and heavy metals, further contribute to oxidative stress and inflammation. Lifestyle factors such as smoking, poor diet, and inadequate sleep exacerbate these effects by impairing barrier function and reducing the skin's regenerative capacity.

Compared to intrinsic aging, extrinsic aging is often more pronounced and is associated with visible clinical features such as hyperpigmentation, coarse texture, and deep wrinkles.

2.3 Molecular and Cellular Mechanisms

At the molecular level, skin aging is governed by a complex network of interconnected processes that disrupt cellular function and tissue structure.

Oxidative stress is a central mechanism, arising from an imbalance between ROS production and antioxidant defenses. Excess ROS damages lipids, proteins, and DNA, leading to impaired cellular function and accelerated aging [1,5].

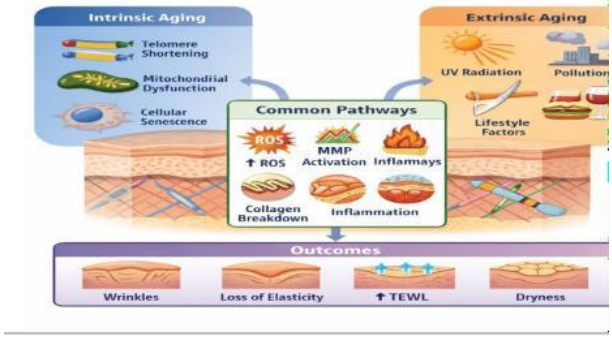
Collagen degradation is another critical process. Matrix metalloproteinases—particularly MMP-1, MMP-3, and MMP-9—are upregulated in response to oxidative stress and UV exposure, resulting in breakdown of collagen fibers and reduced dermal strength and elasticity[1,5,91–93].

Chronic low-grade inflammation, often termed inflammaging, further contributes to tissue damage. Persistent activation of inflammatory pathways leads to sustained release of cytokines and proteases, disrupting normal skin homeostasis.

Barrier dysfunction is also a hallmark of aging skin. Reduced lipid content and compromised stratum corneum integrity increase transepidermal water loss, leading to dryness and decreased hydration. This not only affects skin appearance but also increases susceptibility to environmental insults and microbial invasion[92].

Collectively, these molecular and cellular processes form an integrated network driving skin aging. Advances in biomedical engineering now provide tools to measure, model, and potentially modulate these pathways, enabling more precise and effective anti-aging interventions.

Figure 1. Mechanisms of Skin Aging: Integration of Intrinsic and Extrinsic Pathways



Skin aging is driven by both intrinsic (chronological) and extrinsic (environmental) factors that converge at the molecular and cellular levels. Intrinsic aging is associated with genetic predisposition, telomere shortening, mitochondrial dysfunction, and cellular senescence, leading to reduced collagen synthesis and impaired tissue regeneration. In contrast, extrinsic aging—primarily induced by ultraviolet radiation, pollution, and lifestyle factors—triggers oxidative stress and activates signaling pathways that upregulate matrix metalloproteinases (MMPs), resulting in collagen degradation and extracellular matrix remodeling. Both pathways contribute to chronic low-grade inflammation (inflammaging), barrier dysfunction, and increased transepidermal water loss (TEWL). These processes collectively manifest as wrinkles, loss of elasticity, dryness, and pigmentation changes. The interconnected nature of these mechanisms highlights the complexity of skin aging and underscores the need for systems-level approaches to its assessment and management. measurement of skin barrier function, hydration, biochemical markers, and environmental interactions, offering deeper insight into dynamic physiological changes. As a result, biosensors play an increasingly important role in both clinical research and cosmeceutical development, supporting precise evaluation of skin condition and facilitating data-driven formulation strategies.

Advanced biosensor platforms, including microneedle-based, tattoo-based, and MXene-integrated systems, enable high-sensitivity detection of biochemical markers in aging skin [3,7–9,13,15].

Transepidermal Water Loss (TEWL) Sensors

Transepidermal water loss (TEWL) is a key parameter for assessing skin barrier integrity [2,38]. It quantifies the passive diffusion of water vapor from the skin surface and reflects the functional state of the stratum corneum. Elevated TEWL is associated with impaired barrier function, a hallmark of aging skin characterized by reduced lipid content and structural disorganization [2,43]. TEWL sensors typically operate using open-chamber or closed-chamber diffusion principles, detecting water vapor gradients near the skin surface. Modern devices incorporate miniaturized, high-sensitivity sensors with improved reproducibility, enabling precise quantification of barrier function under varying physiological and environmental conditions [2,6]. In anti-aging research, TEWL measurements are widely used to evaluate the efficacy of topical formulations—such as moisturizers and herbal-based creams—by assessing their ability to restore barrier integrity and reduce water loss. Integration of TEWL sensors into wearable platforms has further expanded their utility, enabling continuous, longitudinal monitoring of skin hydration and barrier recovery in real-world settings.

2.4 Wearable and Flexible Biosensors

Wearable biosensors represent a major advancement in skin monitoring technologies, enabling continuous and non-invasive assessment of physiological parameters. These devices are constructed using flexible, biocompatible materialsthat conform to the skin surface, allowing unobtrusive long-term use. Textile-integrated and flexible sensor systems further enhance long-term monitoring of skin physiological parameters in real-world settings [40–42,44].

Commonly monitored parameters include hydration, pH, temperature, and sebum levels, all of which are influenced by aging processes [6,38,43,45–50]. Flexible electronic systems employ materials such as graphene, conductive polymers, and nanocomposites to achieve high sensitivity and mechanical adaptability [11,45].

These sensors can detect subtle changes in the skin microenvironment, providing insights into dehydration, inflammation, and metabolic activity. In the context of skin aging, wearable biosensors enable personalized monitoring by capturing individual responses to environmental exposure and skincare interventions. When integrated with mobile health platforms, they facilitate real-time data analysis and feedback, supporting the development of personalized and adaptive skincare strategies [12,14,51].

2.5 Optical and Electrochemical Biosensors Optical and electrochemical biosensors provide advanced tools for detecting biochemical markers associated with skin aging.

Optical biosensors—including fluorescence-based and spectroscopic systems—enable non-invasive assessment of parameters such as collagen content, pigmentation, and oxidative stress [5,41]. Techniques such as Raman spectroscopy and diffuse reflectance spectroscopy allow detailed evaluation of the skin's molecular composition [4,10,11].

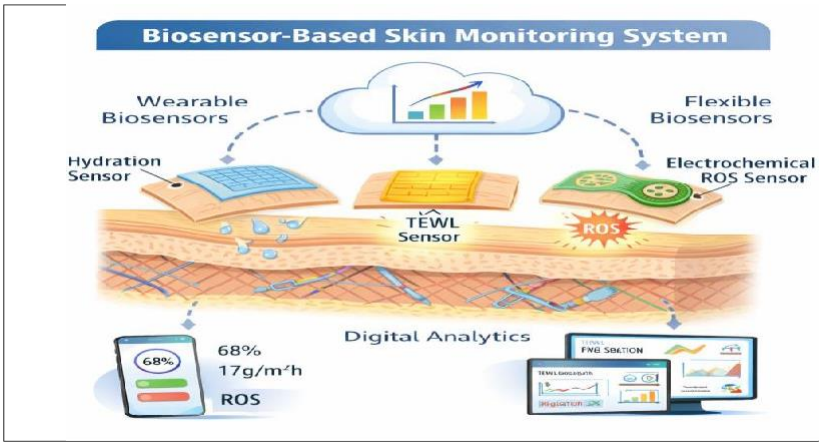
Electrochemical biosensors, in contrast, detect specific biomarkers through redox reactions. These systems can quantify reactive oxygen species (ROS), inflammatory mediators, and enzymatic activity, including matrix metalloproteinases (MMPs) involved in collagen degradation. Their high sensitivity and specificity make them particularly valuable for early detection of molecular changes associated with aging. Recent developments have focused on integrating optical and electrochemical modalities into portable and wearable platforms, enabling simultaneous monitoring of multiple biomarkers [52,53]. Such multimodal systems provide a more comprehensive understanding of skin physiology and bridge the gap between molecular analysis and clinical observation.

2.6 Integration with Digital Health and Data Analytics

The impact of biosensor technologies is significantly enhanced through integration with digital health platforms and advanced data analytics. Data generated from wearable and portable sensors can be processed using machine learning algorithms to identify patterns, predict aging trajectories, and evaluate treatment responses.

This integration enables a shift from reactive to predictive skincare, where interventions are tailored based on individual physiological data. Cloud-based systems and mobile applications support real-time data storage, analysis, and visualization, making biosensor outputs accessible to both researchers and clinicians. Furthermore, these platforms facilitate longitudinal monitoring and large-scale data collection, enabling deeper insights into population-level variability in skin aging and improving the development of personalized cosmeceutical strategies..

Figure 2. Biosensor-based skin monitoring system for real-time assessment of skin aging parameters.



The schematic illustrates the integration of wearable and flexible biosensors for continuous monitoring of skin physiological and biochemical parameters. Sensors positioned on the skin surface measure key indicators such as hydration, transepidermal water loss (TEWL), pH, temperature, and reactive oxygen species (ROS). These data are transmitted to digital platforms, including mobile devices and cloud-based systems, where advanced analytics and machine learning algorithms process and interpret the information.

This integrated framework enables real-time, non-invasive assessment of skin health, supports personalized skincare strategies, and facilitates data-driven evaluation of anti-aging interventions.

3. Advanced Imaging Technologies for Skin Aging Assessment

Advanced imaging technologies have become indispensable tools in dermatological research and clinical practice, enabling non-invasive, high-resolution visualization of skin structure and function [41,57]. Unlike conventional assessment methods that rely on visual inspection or invasive histological analysis, modern imaging techniques provide **quantitative, reproducible, and depth-resolved information** on skin morphology, microarchitecture, and biochemical composition [41].

These technologies are particularly valuable in the study of skin aging, where subtle structural and functional alterations occur across multiple layers of the skin. Biomedical engineering has driven the development of sophisticated imaging modalities capable of characterizing aging-related changes such as collagen degradation, epidermal thinning, and vascular remodeling [54,58].Techniques including **reflectance confocal microscopy (RCM), optical coherence tomography (OCT), and high-resolution digital imaging** have significantly enhanced the ability to monitor skin condition, evaluate treatment efficacy, and investigate underlying aging mechanisms [54–56,81–83].

3.1 Confocal Microscopy

Reflectance confocal microscopy (RCM) is a non-invasive imaging technique that provides real-time visualization of the skin at near-histological resolution. It enables detailed examination of epidermal and superficial dermal structures without the need for tissue biopsy by detecting backscattered light from cellular components [49–53,76].

In the context of skin aging, RCM allows precise assessment of epidermal thickness, keratinocyte morphology, and dermal collagen organization. Age-related changes such as irregular epidermal architecture, reduced cellular density, and fragmentation of collagen fibers can be visualized and quantified.

Additionally, RCM is valuable for monitoring treatment efficacy by enabling direct comparison of skin morphology before and after anti-aging interventions.

3.2 Optical Coherence Tomography (OCT)

Optical coherence tomography (OCT) is a non-invasive imaging modality that utilizes low-coherence interferometry to generate cross-sectional images of the skin. Compared to confocal microscopy, OCT provides greater penetration depth, allowing visualization of both epidermal and dermal layers.

OCT is particularly useful for evaluating structural changes associated with aging, including dermal

thickness, wrinkle formation, and alterations in tissue reflectivity. Quantitative parameters such as layer thickness and optical scattering properties can be derived, providing indirect measures of collagen density and tissue organization.

Recent advancements, including **dynamic OCT and angiographic OCT**, enable visualization of microvascular networks and blood flow within the skin. These features are highly relevant, as vascular alterations contribute to reduced nutrient delivery and impaired tissue repair in aging skin.

3.3 High-Resolution Digital Imaging and Image Analysis

High-resolution digital imaging systems, including dermoscopy and three-dimensional (3D) skin imaging platforms, are widely used to assess surface-level skin characteristics. These systems capture detailed images that can be analyzed using image-processing algorithms to quantify parameters such as wrinkles, pigmentation, and texture.

Three-dimensional imaging provides depth information, enabling accurate measurement of wrinkle depth, skin roughness, and surface topography [1,5,91–93]. These metrics are essential for evaluating the severity of skin aging and the effectiveness of cosmetic or therapeutic interventions.

The integration of digital imaging with computational analysis allows automated and objective skin assessment. Machine learning algorithms can identify aging-related patterns and classify skin types based on morphological features, reducing subjectivity and improving diagnostic accuracy.

3.4 Multimodal Imaging and Integration with Computational Tools

Recent developments in biomedical engineering have focused on integrating multiple imaging modalities to provide a comprehensive assessment of skin structure and function [1,5,91–93]. Multimodal imaging combines techniques such as confocal microscopy, OCT, and spectroscopic analysis to generate complementary datasets spanning cellular, structural, and biochemical levels. When coupled with computational tools and advanced data analytics, multimodal imaging enables the development of predictive models for skin aging. These models integrate imaging data with molecular and environmental inputs, providing a systems-level understanding of skin health.

Such integrated approaches are particularly valuable for personalized skincare, where diagnostic insights can guide tailored therapeutic and cosmeceutical strategies.

4. Microfluidic and Skin-on-Chip Models for Studying Skin Aging

Advances in biomedical engineering have led to the development of microfluidic and organ-on-chip technologies that offer physiologically relevant platforms for studying skin biology and aging [16,20,106]. Traditional in vitro models, such as monolayer cell cultures, and in vivo animal models often fail to replicate the complex architecture and dynamic microenvironment of human skin.

Microfluidic systems and skin-on-chip platforms address these limitations by enabling controlled simulation of skin structure, cellular interactions, mechanical forces, and microcirculation in a highly reproducible manner [20,106–108]. These platforms recreate key features of the skin, including multilayered organization and biochemical gradients, allowing more accurate investigation of aging mechanisms [109–115].

As a result, microfluidic models have emerged as powerful tools for studying skin aging, evaluating cosmeceutical formulations, and analyzing drug delivery and penetration under physiologically relevant conditions.

4.1 Microfluidic Platforms in Skin Research

Microfluidic devices are engineered to manipulate small volumes of fluids within microscale channels, enabling precise control over the cellular microenvironment. In skin research, these systems simulate key physiological processes such as nutrient transport, waste removal, and biochemical gradients that regulate cellular behavior. Microfluidic platforms allow skin cells to be cultured under dynamic conditions, incorporating factors such as shear stress and interstitial fluid flow. These conditions are critical for maintaining cell viability and functionality, particularly in aging studies where alterations in microcirculation and nutrient delivery play a significant role.

In addition, microfluidic systems support high-throughput screening of active compounds, enabling rapid evaluation of multiple formulations under controlled conditions. This capability is especially valuable in cosmeceutical development, where optimization of formulation composition and concentration is required.

4.2 Skin-on-Chip Models

Skin-on-chip systems represent advanced microphysiological platforms that replicate the structural and functional complexity of human skin. These devices typically incorporate multiple layers such as the epidermis and dermis and may include vascular or immune components within a microfluidic framework.

By utilizing human-derived cells, these models provide a more physiologically relevant representation compared to conventional in vitro systems. They enable investigation of key aging-related processes, including collagen degradation, oxidative stress responses, and inflammatory signaling [28].

A major advantage of skin-on-chip systems is their ability to simulate interactions between different cell types, including keratinocytes, fibroblasts, and immune cells. This feature is particularly important in aging research, where cellular cross-talk and

microenvironmental factors significantly influence tissue degeneration and repair.

4.3 Applications in Aging and Cosmeceutical Testing

Microfluidic and skin-on-chip platforms are increasingly applied to evaluate the efficacy and safety of anti-aging formulations. These systems enable controlled testing of active ingredients—including antioxidants, peptides, and plant-derived compounds—under physiologically relevant conditions.

In aging studies, these models can be exposed to environmental stressors such as UV radiation and pollutants to simulate extrinsic aging. The resulting cellular responses, including oxidative stress, inflammation, and extracellular matrix degradation, can be monitored in real time.

These platforms also provide valuable insights into drug penetration and delivery, enabling evaluation of how formulations interact with the skin barrier. This is particularly relevant for advanced delivery systems such as nanoemulsions, liposomes, and hydrogels.

4.4 Integration with Computational and Analytical Tools

The utility of microfluidic and skin-on-chip models is further enhanced through integration with computational and analytical technologies. Data generated from these systems can be analyzed using machine learning algorithms to identify patterns, predict outcomes, and optimize experimental conditions.

Coupling these platforms with imaging techniques and biosensors enables real-time monitoring of cellular and molecular changes. This integrated approach provides a comprehensive understanding of skin aging processes and supports the development of predictive models for treatment efficacy [54,81–83].

Overall, microfluidic and skin-on-chip technologies represent a significant advancement in skin aging research by offering physiologically relevant, highly controlled, and reproducible experimental platforms.

5. Computational Biology and Artificial Intelligence in Skin Aging

Recent advances in computational biology and artificial intelligence (AI) have transformed the study of skin aging by enabling data-driven analysis of complex biological systems. Skin aging is influenced by multifactorial interactions involving genetic, environmental, biochemical, and cellular factors, which are difficult to capture using traditional experimental approaches [54–58,78,88]. AI-driven methodologies—including machine learning, deep learning, and network-based modeling—enable integration of diverse datasets and development of predictive models. These approaches facilitate identification of key biomarkers, prediction of aging trajectories, and optimization of therapeutic and cosmeceutical strategies [59–63,65–69].

5.1 Machine Learning Models for Skin Aging Prediction

Machine learning algorithms are widely used to analyze large-scale datasets derived from imaging, genomics, proteomics, and clinical evaluations. These models can identify patterns associated with skin aging, classify skin types, and predict disease progression or treatment outcomes.

Supervised learning methods, such as support vector machines, random forests, and neural networks, are commonly applied to develop predictive models using labeled datasets. For example, high-resolution skin images can be analyzed to quantify wrinkle depth, pigmentation, and texture, enabling objective assessment of aging severity.

Deep learning approaches—particularly convolutional neural networks (CNNs)—have demonstrated strong performance in automated image analysis. These models can extract complex features and provide accurate classification of skin conditions. Additionally, AI-based “aging clocks” derived from molecular and transcriptomic data enable estimation of biological age and evaluation of intervention efficacy.

5.2 AI-Driven Formulation Design and Optimization

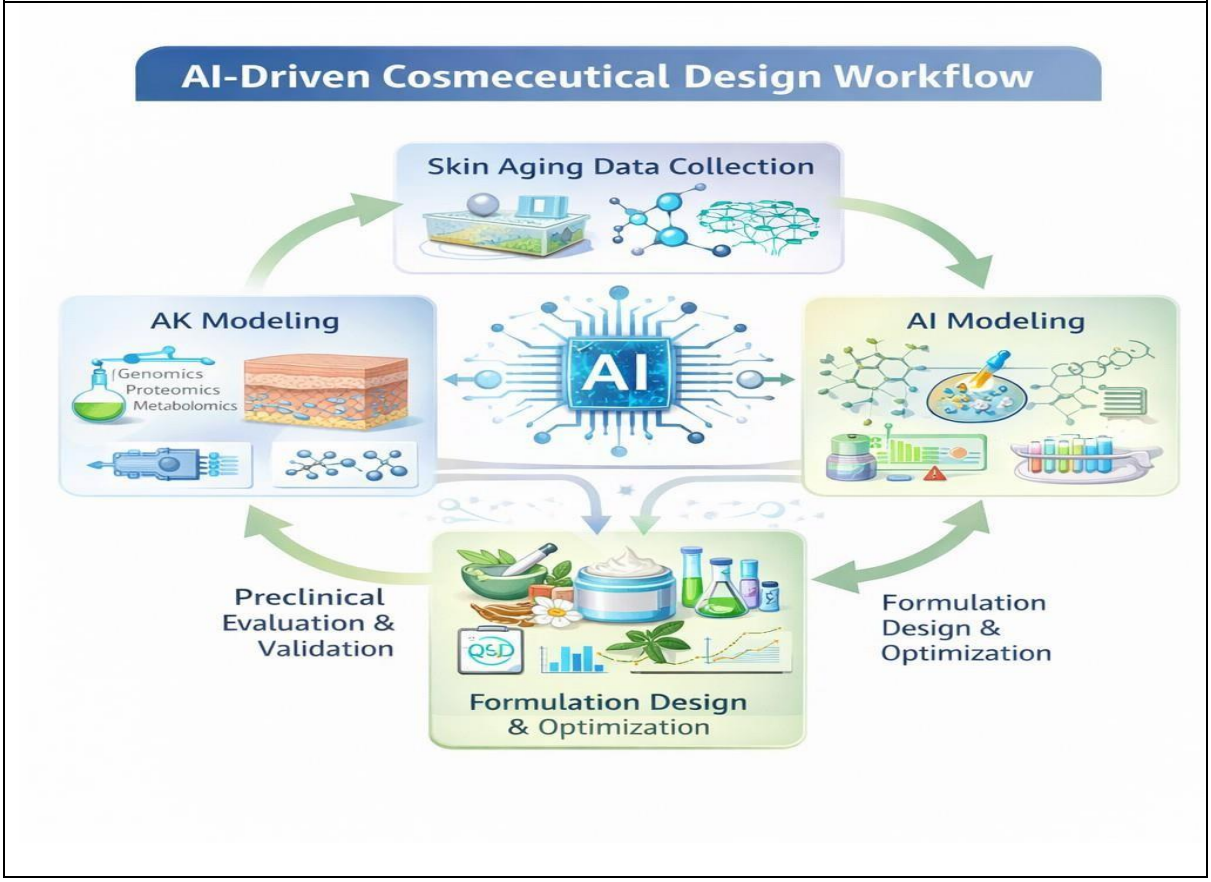
Artificial intelligence is increasingly applied to the design and optimization of cosmeceutical formulations. Traditional formulation development relies heavily on empirical methods and iterative experimentation, which can be time-consuming and resource-intensive. AI-driven approaches enable rapid screening and optimization based on predictive modeling.

Machine learning models can analyze relationships between active ingredients, excipients, and formulation variables to predict stability, efficacy, and skin permeability. This is particularly useful for complex formulations containing multiple bioactive compounds, such as plant-derived flavonoids, where synergistic interactions are critical [64–74].

In anti-aging applications, AI can assist in identifying compounds with antioxidant, anti-inflammatory, and collagen-protective properties. For example, flavonoid-rich extracts containing compounds such as luteolin and vitexin can be computationally evaluated for their potential to inhibit matrix metalloproteinases and reduce oxidative stress [75–79,86–90].

Integration of AI with Quality by Design (QbD) principles further enhances formulation development by enabling systematic evaluation of critical material attributes and process parameters [54–58,62–66]. Predictive models can guide optimization, ensuring product quality, stability, and performance.

Figure 3. AI-driven cosmeceutical design workflow for skin aging applications.



The schematic presents a systems-level workflow integrating artificial intelligence into cosmeceutical development. It begins with comprehensive data acquisition, including clinical parameters, multi-omics datasets, and imaging-derived features. These inputs are processed using AI and machine learning models to identify biomarkers and predict skin responses. The insights are translated into formulation design, guiding the selection of active ingredients, excipients, and delivery systems.

Preclinical validation is conducted using in vitro, ex vivo, and computational models to evaluate efficacy and safety. The workflow operates iteratively, allowing continuous refinement of formulations and enabling the development of personalized, precision skincare solutions.

5.3 Network Pharmacology and Systems-Level Analysis

Network pharmacology adopts a systems biology perspective to understand the multi-target effects of bioactive compounds. Rather than focusing on a single molecular target, it maps interactions between multiple compounds and interconnected biological pathways.

In skin aging research, this approach is especially relevant for plant-based formulations, which contain diverse bioactive constituents [23,24,32]. Computational tools enable mapping of phytochemical–target interactions across pathways involved in oxidative stress, inflammation, and extracellular matrix remodeling.

By constructing interaction networks, key regulatory nodes and pathways can be identified, revealing potential synergistic effects among compounds. This provides a rational foundation for designing multi-component cosmeceuticals and supports evidence-based integration of traditional botanicals with modern therapeutic strategies.

5.4 Integration with Digital Health and Personalized Skincare

The convergence of artificial intelligence with digital health technologies has enabled a shift toward personalized skincare. Data from wearable biosensors, imaging systems, and clinical assessments can be analyzed using AI algorithms to generate individualized recommendations for skincare routines and product selection.

Mobile applications and cloud-based platforms support real-time data processing, allowing users and clinicians to monitor skin health and dynamically adjust interventions. Personalization models incorporate variables such as skin type, environmental exposure, lifestyle factors, and genetic predisposition [36,37,39,86–90].

Predictive simulations further enhance this approach by estimating treatment outcomes before clinical application, reducing reliance on trial-and-error methods and improving development efficiency.

Emerging microbiome-based cosmeceuticals modulate skin barrier function and inflammatory pathways, offering novel anti-aging strategies [88–92].

Collectively, AI and computational biology provide powerful tools for decoding the complexity of skin aging and enabling targeted, personalized cosmeceutical strategies.

6. Cosmeceutical Design Using Biomedical Engineering Approaches

The development of cosmeceuticals has shifted from empirical formulation toward **rational, data-driven design [23,24,32]**. Biomedical engineering principles now enable systematic optimization of formulation performance, stability, and safety through integration of advanced delivery systems, Quality by Design (QbD), and computational tools.

6.1 Advanced Delivery Systems for Anti-Aging Agents

A major challenge in topical formulation is effective delivery of active compounds across the stratum corneum. Advanced delivery systems have been developed to enhance penetration, stability, and controlled release [27,31,35].

Nanotechnology-based carriers—including nanoemulsions, liposomes, solid lipid nanoparticles, and nanostructured lipid carriers—improve solubility and protect bioactives from degradation while enabling targeted delivery to specific skin layers. For example, liposomal systems enhance penetration of antioxidants and peptides, while nanoemulsions improve the bioavailability of hydrophobic compounds such as flavonoids.

Hydrogel-based systems further contribute by providing sustained release, improved hydration, and biocompatibility. These delivery platforms enhance therapeutic efficacy while maintaining favorable sensory properties [27,31,35].

6.2 Quality by Design (QbD) in Cosmeceutical Development

Quality by Design (QbD) provides a systematic framework for ensuring consistent product quality through understanding and control of formulation variables. It involves identifying critical quality attributes (CQAs), critical material attributes (CMAs), and critical process parameters (CPPs).

Design of experiments (DoE) is widely used to evaluate the influence of formulation variables—such as emulsifier concentration, oil phase composition, and processing conditions—on product performance. This approach enables efficient optimization and establishes a robust design space.

Integration of QbD with computational modeling and machine learning further enhances predictive capability, reduces development time, and improves reproducibility, making it a cornerstone of modern cosmeceutical design.

6.3 Herbal and Bioactive-Based Anti-Aging Formulations

Plant-derived bioactives have gained prominence due to their antioxidant, anti-inflammatory, and collagen-protective properties. Classes such as flavonoids, polyphenols, and terpenoids modulate key aging pathways, including oxidative stress and matrix degradation.

Biomedical engineering tools facilitate systematic evaluation of these compounds. Techniques such as molecular docking, network pharmacology, and enzyme inhibition assays help identify active molecules and predict their biological interactions.

For instance, flavonoids such as luteolin and vitexin have demonstrated potential to inhibit collagenase activity, supporting their role in anti-aging formulations [26]. When combined with advanced delivery systems, their stability and bioavailability are significantly enhanced, enabling more effective therapeutic outcomes [28].

6.4 Integration with AI and Precision Cosmeceuticals

Artificial intelligence is driving the transition toward precision cosmeceuticals. AI-driven platforms can integrate data from biosensors, imaging, and molecular studies to predict individual skin responses and guide formulation design.

Predictive models enable selection of optimal ingredient combinations and delivery systems tailored to specific skin profiles. This reduces reliance on empirical testing and accelerates formulation development [39].

Integration with digital health systems allows continuous monitoring and adaptive adjustment of skincare interventions in real time. This convergence of AI, biomedical engineering, and dermatological science is establishing a new paradigm in skincare—where treatments are personalized, predictive, and dynamically optimized.

Table 1. Comparative overview of biomedical engineering technologies applied in skin aging research and cosmeceutical development.

Technology Category	Key Techniques / Tools	Parameters Measured / Analyzed	Applications in Skin Aging	Advantages	Limitations
Biosensors	TEWL sensors, wearable sensors, electrochemical sensors	Hydration, TEWL, pH, ROS, temperature	Real-time monitoring of skin barrier function and	Non-invasive, continuous monitoring, portable	Calibration variability, limited depth resolution

			biochemical status		
Imaging Technologies	Confocal microscopy, optical coherence tomography (OCT), 3D imaging	Skin thickness, collagen structure, wrinkles, pigmentation	Structural and morphological assessment of aging skin	High resolution, non-invasive, quantitative analysis	High cost, requires technical expertise
Microfluidic & Skin-on-Chip Models	Lab-on-chip systems, organ-on-chip platforms	Cellular interactions, barrier function, drug penetration	Mechanistic studies and cosmeceutical testing	Physiologically relevant, controlled microenvironment	Complex fabrication, limited scalability
Computational Biology & AI	Machine learning, deep learning, network pharmacology	Multi-omics data, imaging data, biomarker prediction	Aging prediction, pathway analysis, formulation optimization	Predictive modeling, systems-level insights	Requires large datasets, validation challenges
Cosmeceutical Engineering	QbD, nanocarriers (liposomes, nanoemulsions), hydrogels	Stability, permeability, efficacy, release profile	Development of targeted anti-aging formulations	Enhanced delivery, improved bioavailability	Regulatory complexity, formulation challenges

7. Challenges and Limitations in Biomedical Engineering Approaches to Skin Aging

Despite rapid advancements in biomedical engineering technologies for skin aging research and cosmeceutical development, several challenges continue to limit their full potential [96–100]. These arise from biological complexity, technological constraints, data integration issues, regulatory gaps, and translational barriers [97,98].

7.1 Biological Complexity and Variability

Skin aging is inherently heterogeneous, influenced by genetic background, environmental exposure, ethnicity, and lifestyle. This variability complicates the development of universally applicable models and formulations.

Additionally, the skin's multilayered structure involves complex interactions between epidermal, dermal, and immune components. Although advanced models such as skin-on-chip systems improve physiological relevance, they still fall short of replicating systemic influences such as hormonal signaling and immune responses.

7.2 Limitations of Current Technologies

Biosensors and imaging systems provide non-invasive and real-time insights but are not without limitations. Biosensors are often restricted to surface-level measurements and may not fully capture deeper dermal processes. Factors such as calibration drift, signal interference, and environmental variability can affect measurement accuracy.

Advanced imaging modalities offer high-resolution structural data but are costly and require specialized expertise. Despite progress in automated analysis, interpretation can still be operator-dependent.

Microfluidic and organ-on-chip platforms, while promising, involve complex fabrication and infrastructure requirements. Their scalability for industrial and large-scale applications remains a key limitation.

7.3 Data Integration and Computational Challenges

The integration of multi-omics, imaging, and biosensor data presents significant computational challenges. Handling large, heterogeneous datasets requires robust infrastructure and advanced analytics.

Machine learning models are highly dependent on data quality and diversity; biased or insufficient datasets can lead to unreliable predictions. Moreover, the "black-box" nature of many AI models limits interpretability, which poses challenges for clinical acceptance and regulatory approval.

7.4 Regulatory and Standardization Issues

The rapid emergence of technologies such as nanocarriers, AI-driven formulations, and wearable biosensors has outpaced existing regulatory frameworks. Lack of standardized guidelines for testing, validation, and performance assessment creates barriers to product approval and commercialization.

Harmonization of protocols and evaluation metrics is essential to ensure reproducibility, comparability, and consumer safety across global markets.

7.5 Translation to Clinical and Commercial Applications

A persistent challenge lies in translating laboratory

findings into real-world applications. Technologies that perform well under controlled conditions may exhibit variability in clinical or consumer environments due to differences in usage patterns and environmental exposure.

Cost and scalability further influence adoption. High development and manufacturing costs may limit accessibility, particularly in consumer-focused skincare markets.

Overall, addressing these challenges will require interdisciplinary collaboration, technological innovation, and regulatory evolution to enable reliable, scalable, and clinically relevant solutions.

8. Future Perspectives in Biomedical Engineering for Skin Aging

The convergence of biomedical engineering, computational biology, and dermatological science is poised to transform skin aging research from descriptive and reactive approaches to predictive, preventive, and personalized strategies.

8.1 AI-Driven Precision Skincare

Artificial intelligence will play a central role in future skincare systems by integrating data from biosensors, imaging platforms, genetic profiling, and environmental monitoring [86–90]. These systems will generate comprehensive individual skin profiles, enabling prediction of aging trajectories and personalized intervention strategies.

Advances in explainable AI are expected to improve model transparency, facilitating clinical acceptance. Real-time adaptive systems may continuously refine treatment strategies based on dynamic skin responses.

8.2 Integration of Multi-Omics and Systems Biology

Multi-omics approaches—including genomics, proteomics, metabolomics, and transcriptomics—will deepen understanding of molecular aging mechanisms. These data, when integrated into systems biology frameworks, will allow identification of novel biomarkers and therapeutic targets.

This approach supports the development of multi-target cosmeceuticals that address interconnected pathways, improving efficacy and long-term outcomes.

8.3 Smart Wearable and Implantable Devices

Future biosensor technologies will extend beyond wearables to include implantable systems capable of continuous monitoring of biochemical and physiological parameters. These devices will leverage flexible electronics, nanomaterials, and wireless communication for seamless integration with digital health platforms.

Such systems will enable early detection of skin changes, continuous monitoring of treatment response, and proactive intervention strategies.

8.4 Advanced In Vitro Models and Digital Twins

Next-generation microphysiological systems will incorporate vascular, immune, and neural components to more accurately replicate human skin.

The concept of digital twins—virtual representations of biological systems—will enable simulation of skin behavior under varying conditions. These models can predict treatment outcomes, optimize formulations, and reduce reliance on experimental testing.

8.5 Sustainable and Green Cosmeceutical Development

Sustainability will play an increasingly important role in future cosmeceutical design. Emphasis will shift toward biodegradable materials, eco-friendly delivery systems, and ethically sourced natural ingredients.

Biotechnological production methods, such as plant cell culture and microbial synthesis, will enable sustainable manufacturing of bioactive compounds. Integration of green chemistry principles with biomedical engineering will support environmentally responsible innovation.

8.6 Regulatory Evolution and Standardization

Regulatory frameworks will need to evolve to address emerging technologies, including AI-based systems, nanotechnology, and bioengineered products. Establishing standardized validation protocols and safety guidelines will be critical. Collaboration among academia, industry, and regulatory bodies will be essential to balance innovation with safety and compliance. Collectively, these developments indicate a shift toward precision, predictive, and sustainable skincare paradigms, driven by technological convergence.

9. Conclusion

Skin aging is a complex, multifactorial process governed by the interplay of intrinsic biological mechanisms and extrinsic environmental factors. Conventional approaches, largely based on observational and empirical strategies, have limited capacity to address this complexity.

The integration of biomedical engineering technologies—including biosensors, advanced imaging systems, microfluidic platforms, and AI-driven computational models—has fundamentally transformed the field. These tools enable quantitative, systems-level analysis of skin structure and function, facilitating real-time monitoring, high-resolution visualization, and predictive modeling.

Furthermore, the application of engineering principles to cosmeceutical design—through advanced delivery systems, Quality by Design frameworks, and AI-based optimization—has enabled the development of targeted, reproducible, and high-performance formulations. The incorporation of plant-derived bioactives, supported by computational and experimental validation, highlights the value of integrating traditional knowledge with modern scientific approaches.

Despite these advances, challenges related to

biological variability, technological limitations, data integration, and regulatory frameworks remain. Addressing these barriers will require continued interdisciplinary collaboration and innovation.

Looking ahead, the convergence of biomedical engineering, artificial intelligence, and dermatological science is expected to drive the transition toward precision and personalized skincare [101–108]. Future innovations in wearable diagnostics, digital health platforms, and predictive modeling will enable proactive, individualized management of skin aging.

Ultimately, these advancements will redefine cosmeceutical research, shifting the paradigm from reactive treatment toward predictive, preventive, and data-driven care.

Declarations

Ethics approval and consent to participate

This piece serves as a review, so it includes neither human nor animal subjects. Participation of living beings falls outside its scope.

Consent for publication

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