ual: london college of fashion

fashion business school

Holistic Sustainability in the Anti-Ageing Market:

Bakuchiol's Future as a Functional Retinoid Alternative

Kit Palermo

20017232

MSc Cosmetic Science

Year 4

MSc Project for Cosmetic Science

Word count: 14,181 words Dissertation

Academic year 2024 - 2025

Table of Contents

Statement of Originality0

Acknowledgements0

Abstract0

Table of Acronyms Used0

I. Introduction1
II. Aims & Objectives3
    a. Aims3
    b. Objectives3
III. Methods3
IV. Ageing5
    a. Skin Ageing Mechanisms & Pathways5
        i. Intrinsic & Extrinsic Ageing5
        ii. Cellular Senescence & Menopause6
        iii. Collagen Degradation8
        iv. Elastin Destruction11
        v. Extracellular Matrix Damage12
        vi. Skin Barrier Damage14
        vii. Glycation15
        viii. MMPs, UVR, and Free Radicals15
        ix. Inflammation17
        x. Hyperpigmentation18
    b. Ageing Summary19
V. Retinoids20
    a. Retinoids Overview20
    b. Mechanisms of Action21
    c. Retinoid Benefits21
        i. Keratinisation21
        ii. Collagen22
        iii. Elastin22
        iv. Extracellular Matrix25
        v. MMPs, UVR, and Free Radicals26
        vi. Hyperpigmentation26

d. Retinoid Issues28
    i. Skin Barrier Damage28
    ii. Glycation29
    iii. Inflammation30
    iv. Photosensitivity & Instability32
    v. Systemic Absorption & Safety33
e. Retinoid Summary35

I. Holistic Sustainability35
a. Consumer Behaviour & Market Research35
b. Business Sustainability & Consumer Influence37

I. Bakuchiol40
a. Bakuchiol Overview40
b. Retinoid Comparison42
    i. Anti-Ageing42
        1. Collagen42
        2. Antioxidant Behaviour43
        3. Inflammation43
        4. Hyperpigmentation44
    ii. Anti-Acne45
        1. Sebum Alteration45
        2. Anti-Bacterial Activity46
    iii. Concentration Regulations47
    iv. Sourcing48

I. Conclusions48

II. References50

Statement of Originality

I, Kit Palermo, certify that this is an original piece of work. I have acknowledged all sources and citations. No section of this report has been plagiarised.

Acknowledgements

In the writing of this dissertation, I have received assistance from Adrienne Palermo, Milica Stevic, Jack O'Grady, and UAL Disability Services. Adrienne Palermo, Milica Stevic, and Jack O'Grady provided feedback, proofread, and helped edit this review paper.

Abstract

This dissertation investigates the convergence of dermatological science, consumer behaviour, and sustainability within the anti-ageing skincare sector, focusing on retinoids and the plant-derived alternative, bakuchiol. Through a narrative review of scientific literature, market reports, and consumer data, the research examines the biological mechanisms of skin ageing, including collagen degradation, elastin breakdown, cellular senescence, and chronic inflammation, before evaluating the efficacy and limitations of retinoids as the current "gold standard". While retinoids demonstrate robust anti-ageing benefits via collagen synthesis, epidermal renewal, and extracellular matrix preservation, they are also associated with irritation, barrier impairment, photoinstability, and sustainability concerns due to their synthetic production processes. Bakuchiol, in contrast, is presented as a bioactive with similar dermal benefits, such as collagen promotion, antioxidant action, and anti-inflammatory effects, yet with lower irritancy potential and a more sustainable sourcing profile. The analysis situates these actives within shifting consumer priorities shaped by post-pandemic scepticism, "clean beauty" trends, and demands for ethical, transparent, and ecologically responsible products. Findings reveal a disconnect between these values and prevailing industry practices, particularly in sourcing ethics and environmental accountability. The review concludes that integrating a holistic model of sustainability, encompassing environmental, social, and economic dimensions, into cosmetic formulation and marketing could bridge this gap. Bakuchiol emerges as a promising exemplar for future innovation, offering a path toward high-performance skincare aligned with evolving consumer ethics and planetary health.

Table I - Table of Acronyms Used

Acronyms & Shorthands	What it means
UVR/UVA/UVB	Ultraviolet Radiation/A/B
DNA	Deoxyribonucleic Acid
ECM	Extracellular Matrix
HRT	Hormone Replacement Therapy
DHEA	Dehydroepiandrosterone
AP-1	Activator Protein-1
TGF-β	Transforming Growth Factor-Beta
MMPs	Matrix Metalloproteinases
TβRI/TβRII	Transforming Growth Factor-Beta receptor I/II
SC	Stratum Corneum
TEWL	Transepidermal Water Loss
AGEs	Advanced Glycation End-Products
ROS	Reactive Oxygen Species
PIH	Post-Inflammatory Hyperpigmentation
RARα, RARβ, RARγ, RXRα, RXRβ, RXRγ	RA Receptor α/β/γ and Retinoic X Receptor α/β/γ
ATRA	Tretinoin/All-Trans Retinoic Acid
RA	Retinoic Acid
RAREs	Retinoic Acid Response Elements
MMP-1, MMP-3, and MMP-9	Collagenase/ Stromelysin/ Gelatinase
ELISA	Enzyme-Linked Immunosorbent Assay
HPR	Hydroxypinacolone Retinoate
TIMPs	Tissue Inhibitors of Metalloproteinases
RAGE	receptor for AGEs
OTC	Over-The-Counter
RBPs, CRBPs, CRABPs	Retinoid-Binding Proteins/ Cellular Retinol-Binding Proteins/ Cellular Retinoic Acid-Binding Proteins
COVID-19	Coronavirus Disease 2019
CSR	Corporate Social Responsibility
MIF	Migration Inhibitory Factor
IL-8	Interleukin-8
DHT	Dihydrotestosterone

I. Introduction

The skincare industry has witnessed marked growth in the post-pandemic era, largely driven by a surge in consumer emphasis on self-care, product safety, and well-informed purchasing decisions. The COVID-19 pandemic intensified health-related anxieties, leading to heightened scepticism not only toward traditional medical advice but also toward the ingredients and practices associated with personal care products. In response, many consumers began gravitating toward “clean,” “green,” or “natural” beauty formulations, which are widely perceived as safer, more ethical, and more transparent than synthetic alternatives (Officer, 2023).

At the heart of this shift lies a more empowered and inquisitive consumer. Increased access to information, primarily through social media, blogs, and other informal digital channels, has cultivated a base of consumers who are not only more aware of what they apply to their skin, but also increasingly critical of the motivations and practices of the brands they support (Dlamini & Mahowa, 2024). Although such platforms are valuable tools for democratizing information, they often disseminate content lacking scientific rigor, giving rise to widespread misconceptions. Nevertheless, this demand for transparency and ingredient literacy has created a ripple effect across the skincare landscape. In some instances, consumer pressure has compelled brands to reformulate products, redesign supply chains, and adopt more ethical business practices to remain competitive (Kapoor *et al.,* 2019).

These transformations in consumer awareness intersect profoundly with evolving cultural narratives around ageing and physical appearance. Historically, reaching old age was a rare achievement, constrained by limited medical knowledge and harsher living conditions. As advances in healthcare and societal infrastructure have significantly extended life expectancy, ageing has paradoxically become both more common and, in many Western societies, less socially desirable. While ageing is still associated with wisdom and personal growth in many cultures, physical manifestations of ageing, such as wrinkles, age spots, and greying hair, are often framed as aesthetic liabilities. This reflects a deeper tension in Western contexts, where physical appearance remains closely tied to perceived social value and economic opportunity (Heilman & Stopeck, 1985).

Youthfulness is frequently equated with vitality, productivity, and cultural relevance, which are traits that can directly impact one’s social standing and professional advancement. As a result, visible signs of ageing can adversely affect self-esteem, interpersonal relationships, and career prospects (Farris & Rendon, 2010; Fisher *et al.,* 1996). Compounding this issue is the evolving

definition of “visible ageing,” which increasingly encompasses concerns among younger demographics. Demand for preventative aesthetic interventions, such as chemical peels, laser treatments, and even surgery, is rising among Millennials and male consumers alike (Sherber, 2018). Social media platforms, while offering spaces for community-building and self-expression, also reinforce unrealistic beauty standards, contributing to widespread dissatisfaction and body dysmorphia (Wang *et al.,* 2019).

These sociocultural pressures have driven the rapid growth of the anti-ageing sector, which is now valued at nearly $10 billion globally (Yaar & Gilchrest, 2007). Notably, much of this market is dominated by non-invasive, topical solutions, underscoring a strong consumer preference for accessible, lower-risk interventions that delay or mask visible signs of ageing. This emphasis on safety and efficacy aligns with the broader trend of consumer education, as individuals increasingly seek out products that not only deliver results but also align with their personal values regarding health, sustainability, and ethical production.

These evolving expectations are particularly paramount in the anti-ageing skincare category, which represents one of the most innovation-driven segments of the beauty industry. The scale and profitability of this market make it an ideal testing ground for sustainable and ethical product development. As consumer scrutiny intensifies, the demand for high-performing actives that also reflect broader social and environmental values continues to rise (Shahzad *et al.,* 2024).

Retinoids have been long regarded as the “gold standard” in anti-ageing and acne treatment. Biologically, retinoids work by stimulating fibroblasts to increase collagen production and accelerating epidermal turnover, resulting in improved skin tone, smoother texture, and reduced fine lines (Brown *et al.,* 2023). Their multifunctionality appeals to modern consumers who value streamlined, efficient routines. However, despite their demonstrated efficacy, retinoids are often associated with side effects such as irritation, dryness, sensitivity, and temporary acne flares, making them less suitable for sensitive skin types or for individuals seeking gentler options (Dlamini & Mahowa, 2024; Trompezinski *et al.,* 2016).

The limitations of retinoids, alongside growing consumer knowledge and value-based purchasing habits, have led to increased interest in plant-based alternatives. Among these, bakuchiol, a phytochemical derived from the seeds and leaves of *Psoralea corylifolia* that is native to Southeast Asia, has emerged as a particularly promising compound. Although structurally distinct from retinoids, bakuchiol exhibits functional similarities, particularly in promoting collagen synthesis and improving skin elasticity. Its lower potential for irritation, combined with its botanical

origin, and the possibility for “greener” extraction methods, aligns well with the evolving priorities of educated, health-conscious, and environmentally aware consumers. In this context, bakuchiol serves as a valuable case study through which to explore how safety, efficacy, and sustainability can converge in the development of next-generation skincare products (Putriana et al., 2024).

II. Aims & Objectives

a. Aims

The aim of this review is to use various online databases and search engines to review research and information regarding retinoids and bakuchiol, with a focus on efficacy, function, and holistic sustainability.

b. Objectives

1. Identify guiding research questions and search criteria.
2. To gather sources from various online databases of academic media.
3. To give background for the anti-ageing market, past and current consumer behaviour.
4. To explain ageing from a biological perspective.
5. To introduce retinoids and how they combat ageing signs, including its shortcomings.
6. To understand the disconnect between ethical consumer behaviour and current business sustainability practices and suggest changes to be made in the market.
7. To introduce bakuchiol, compare its functions with similar ones in retinoids, and explain where it exceeds them.
8. To provide evidence for bakuchiol as a more widely used retinoid alternative and call for more research in this area.

III. Methods

Conducted preliminary research on research topic through secondary sources on vitamin A, retinoids, bakuchiol, current sustainability practices, and current consumer behaviour. Identified research questions, listed below:

1. What is ageing scientifically? Why is anti-ageing a needed sector of the market?
2. How does retinol work to combat ageing? What are its current issues?
3. What is bakuchiol? How do retinoids and bakuchiol compare to each other? Does it excel in areas retinoids don’t?
4. What does consumer behaviour say about how companies market, practice, and listen to consumers? What are ways for companies to behave more ethically, and in line with consumer behaviour?

Then completed a narrative review of PubMed, Wiley Online Library, and Google Scholar using the key search terms outlined in Table II. The inclusion and exclusion criteria for sources involved in the search are listed in Table III. Sources used that were published before 2015 are included because they are foundational articles that are heavily sourced in contemporary reviews, studies and clinicals. The similar information found in contemporary research didn't explain or expand on the older concepts in a way that was beneficial to this research, and it's aims. Review papers were used to identify further primary and notably important sources. Research questions were directly used to confirm if source was of note, as much of research on retinoids discussed vitamin A in other areas of the body like the liver or lungs. The final group of sources was thoroughly reviewed with the designated research questions that guided the context of the review. Finally, the review was structured, compiled, and written from a holistically sustainable lens, to show the promise of bakuchiol in research and at a larger market scale.

Table II – Key Search Terms

First Search Term	Boolean Operator	Second Search Term	Boolean Operator	Third Search Term	Boolean Operator	Fourth Search Term
Retinoid(s)	AND	"Anti-Ageing" / "Skin Ageing"	AND	"Collagen" / "Collagen Proliferation" / "Cell Turnover"	OR	"Irritation" / "Photoageing" / "Ageing Mechanism(s)"
Retinol		"Skin Ageing" / "Visible Ageing"		"Mechanism" / "Pathway"		"Clinical Efficacy" / "Side Effects"
Bakuchiol		"Structure" / "Function" / "Plant-Based Retinoid Alternative"		"Retinoid Comparison" / "Anti-Bacterial" / "Anti-Acne" / "Anti-Ageing"		"Natural Retinoid" / "Mechanism(s)"
Consumer Behaviour		"Green Purchasing Behaviour"		"Ethics" / "COVID-19" / "Brand Trust"		"Social Media" / "Transparency" / "Clean Beauty"
Sustainability		"Cosmetics Industry"		"Ethical Sourcing" / "Holistic Sustainability"		"Development Goals" / "Business Practices" / "Economic Viability"

Table III – Inclusion and Exclusion Search Criteria

Inclusion Criteria	Exclusion Criteria
Articles and abstracts available in English	Articles not published in English
Peer-reviewed case studies, journals, clinicals and articles	Websites (certain web pages included as they list government regulations or vital information)
Published between 1974 and 2025	Sources published before 1974
Studies focused on retinoids, bakuchiol, ageing, and concentration regulations	Articles unrelated to skincare, anti-ageing, holistic sustainability or business practices and sourcing
Sources addressing holistic sustainability, consumer purchasing behaviour, and current business practices	Duplicated or irrelevant research (i.e. medical research not pertaining to dermatology)

IV. Ageing

a. Skin Ageing Mechanisms & Pathways

i. Intrinsic & Extrinsic Ageing

It is essential to establish a comprehensive understanding of the mechanisms and manifestations of skin ageing to gain context for this review. Ageing is a complex, multifactorial process that affects nearly all physiological systems in the body. Common systemic changes include joint stiffness, diminished visual acuity, and alterations in physical appearance. Among these, the skin is particularly susceptible to visible and functional changes, making it both a marker and a site of ageing.

Cutaneous ageing presents through a variety of clinical and histological features, including the development of fine lines and wrinkles, loss of dermal firmness and elasticity, increased dryness, uneven pigmentation, inflammation, altered surface texture, delayed wound healing, and a progressive reduction in subcutaneous fat (Chen *et al.,* 2012; Fisher *et al.,* 1997). These changes reflect both structural degradation and functional decline within the skin's layered architecture, and they significantly impact not only aesthetic appearance but also skin barrier integrity and resilience.

In dermatological literature, skin ageing is typically classified into two primary categories: intrinsic and extrinsic. Intrinsic ageing encompasses the genetically determined, endogenous processes that unfold with time. These include telomere shortening, reduced stem cell renewal, hormonal changes, such as menopause, and the gradual onset of cellular senescence. Intrinsic

ageing tends to manifest more prominently in later life, typically becoming more pronounced around the age of 70, and is considered largely inevitable (Watson *et al.,* 2015).

Conversely, extrinsic ageing refers to age-accelerating influences arising from environmental exposures and lifestyle choices. These external factors interact with the skin to intensify or hasten the intrinsic ageing process, often leading to premature and more severe manifestations of visual ageing. Ultraviolet radiation (UVR) remains the most significant contributor, inducing oxidative stress, DNA damage, and matrix degradation. Additional extrinsic factors include air pollution, tobacco smoking, and nutritional deficiencies, all of which compound the deterioration of dermal structures and functions (Watson *et al.,* 2014).

Understanding the dual nature of skin ageing is critical to contextualizing the role of retinoids, which are uniquely positioned to target both intrinsic and extrinsic pathways. By modulating cellular processes and promoting structural regeneration, retinoids offer a scientifically validated means of mitigating the clinical signs of ageing. This aligns both with medical dermatology and contemporary consumer demands for effective, evidence-based skincare.

i. Cellular Senescence & Menopause

Intrinsic ageing is a gradual, genetically programmed biological process governed by internal physiological mechanisms that lie largely beyond human control. It encompasses the progressive decline in cellular function, diminished tissue regeneration, and alterations in systemic hormonal regulation. While often perceived through a cosmetic lens, intrinsic ageing holds increasing clinical and functional significance, particularly considering the rising global life expectancy. As individuals live longer, the physiological consequences of cutaneous ageing, once seen as superficial, are now recognized for their broader implications on skin health, wound healing, and overall quality of life.

At the cellular level, one of the central hallmarks of intrinsic ageing is the accumulation of senescent cells, cells that have permanently exited the cell cycle in response to replicative exhaustion or various forms of cellular stress (Lemaitre, 2024). While cellular senescence serves an essential tumour-suppressive role by preventing the propagation of damaged DNA, its long-term persistence disrupts tissue homeostasis. Senescent cells develop a pro-inflammatory secretory profile characterized by elevated levels of cytokines, chemokines, proteases, and growth factors (Asl *et al.,* 2021; Campisi & d'Adda di Fagagna, 2007). In the skin, this leads to a decrease in the biosynthesis of key extracellular matrix (ECM) components, particularly collagen and elastin,

contributing to hallmark features of aged skin such as dermal thinning, impaired wound healing, and wrinkle formation (Baker *et al.,* 2023).

A key upstream driver of senescence is telomere shortening. Telomeres are repetitive nucleotide sequences located at chromosomal ends that preserve genomic integrity during cell division. However, due to the end-replication problem inherent to DNA polymerases, telomeres progressively shorten with each mitotic cycle. When critically short, cells either enter senescence or undergo apoptosis, programmed cell death (Blasco, 2007). This phenomenon significantly reduces the proliferative capacity of essential skin cells such as keratinocytes and fibroblasts, thereby impairing the skin's ability to repair and renew itself over time (Kawanishi & Oikawa, 2004).

Hormonal regulation represents another pivotal dimension of intrinsic ageing, particularly in relation to postmenopausal skin physiology. The decline in oestrogen during menopause, typically occurring between the ages of 45 and 55, is one of the most significant endocrine changes affecting female skin. As ovarian follicles become unresponsive, oestrogen production sharply declines, leading to substantial reductions in collagen synthesis, dermal hydration, and elasticity (Lephart, 2018; Stanczyk, 2009; Colombo *et al.,* 2025). Studies suggest that up to 30% of collagen is lost within the first four years following menopause, with an additional 2% decline annually thereafter (Zouboulis, 2003). Given that oestrogen regulates a range of skin cell types, including fibroblasts, keratinocytes, and melanocytes, its depletion compromises ECM integrity, reduces antioxidant capacity, and heightens vulnerability to oxidative damage (Son *et al.,* 2020). These hormonal shifts culminate in characteristic signs of postmenopausal skin: dryness, thinning, decreased elasticity, and reduced resilience (Brincat *et al.,* 1983; Lephart & Naftolin, 2020; Zouboulis & Makrantonaki, 2012).

While hormone replacement therapy (HRT) has been investigated as a strategy for mitigating these effects, its efficacy appears to be site-specific and dependent on the extent of photoageing. For instance, although HRT has demonstrated improvements in collagen synthesis and hydration in sun-protected skin, results have been inconsistent in photoaged areas, highlighting the complex interplay between intrinsic and extrinsic ageing mechanisms (Bolognia *et al.,* 1989; Schmidt *et al.,* 1997; Rittie *et al.,* 2008).

Although less dramatic than oestrogen, testosterone also contributes to skin health, particularly through its effects on sebum production and skin thickness. In both men and women, age-related declines in testosterone are associated with increased dryness and reduced structural

integrity of the skin (Zouboulis & Makrantonaki, 2012). Additional hormones, like growth hormone and dehydroepiandrosterone (DHEA), further influence skin ageing. Growth hormone supports cellular regeneration, while DHEA, an androgen precursor, enhances barrier function and sebum production. The cumulative decline of these hormones with age exacerbates the structural and functional deterioration of the skin, intensifying both the visible and subclinical manifestations of intrinsic ageing (Ganceviciene *et al.,* 2012).

i. Collagen Degradation

Collagen and elastin, the principal structural proteins of the dermal ECM, are synthesized by fibroblasts and play a foundational role in maintaining the skin's tensile strength, elasticity, and biomechanical resilience. Collagen, a fibrous protein composed of criss-crossed fibrils, constitutes up to 80% of the skin's dry weight and provides the scaffolding necessary for dermal integrity. This network not only confers structural stability but also facilitates the binding of other ECM components, thereby reinforcing the skin's mechanical properties and intercellular communication (Amirrah *et al.,* 2022).

Among the various collagen types present in human skin, Types I, III, IV, and VII are of importance to ageing, with Type I being the most prevalent, comprising nearly 90% of total dermal collagen. The biosynthesis of Type I collagen is a complex, multi-step process that begins intracellularly with the transcription of the proα1(I) and proα2(I) genes. These transcripts are translated into pre-procollagen chains in the cytoplasm, which then undergo extensive post-translational modifications in the endoplasmic reticulum to form the characteristic triple-helix structure of procollagen. Following Golgi-mediated processes, procollagen is secreted into the extracellular space, where peptidases cleave its terminal regions to produce tropocollagen. This is subsequently cross-linked by lysyl oxidase to form mature collagen fibrils that integrate into the ECM scaffold (Prockop, 1982). See Figure 1 for a visualisation of the intracellular collagen synthesis process, as well as the extracellular process and post-translational modifications. This process acts as a vital, if not the most important, aspect of dermal structure, and changes to this process can be detrimental.

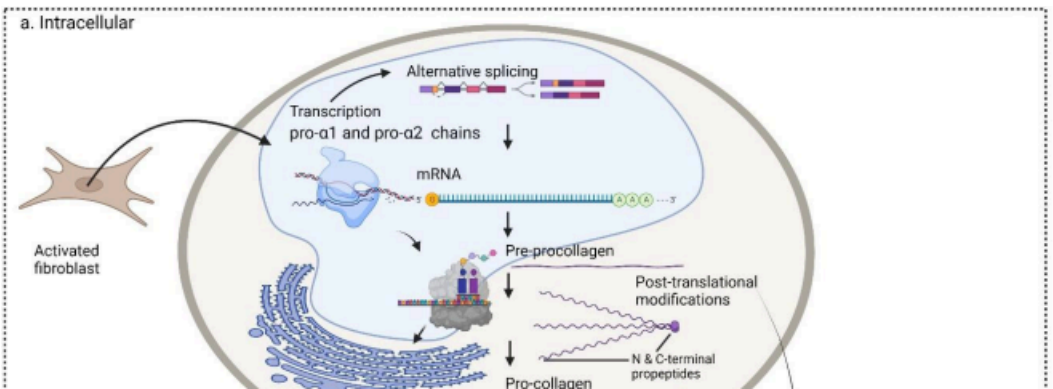


Figure 1: Overview of collagen type I biosynthesis from (a) intracellular transcription to (b) formation of extracellular complex macromolecular structures and what happens in between during (c) posttranslational modifications (Source: Amirrah *et al.,* 2022).

In youthful, photo-protected skin, fibroblasts anchored to intact collagen fibrils exert mechanical tension on the ECM, thereby maintaining collagen homeostasis through continuous synthesis and matrix remodelling. However, with advancing age, particularly under the influence of extrinsic stressors such as UVR, this balance is disrupted. UVR induces oxidative stress leading to fragmentation and disorganization of collagen fibrils. This degradation alters fibroblast-ECM interactions, impairing mechanotransduction and triggering a phenotypic shift in fibroblasts from matrix synthesis to matrix degradation (Fisher *et al.,* 2009; Fisher *et al.,* 2013).

Collagen fragmentation emerges as a pivotal feature of both intrinsic and extrinsic ageing, undermining dermal structure and fibroblast functionality. Over time, the accumulation of fragmented collagen fibrils creates a feedback loop characterized by increased degradation and suppressed synthesis, thereby accelerating dermal thinning and the emergence of clinical signs of ageing, such as wrinkles and loss of structure (Bornstein, 1974; Chung *et al.,* 1996).

At the molecular level, transcription factors such as activator protein-1 (AP-1) are instrumental in regulating the balance between collagen production and degradation. AP-1 is upregulated in response to UVR and exerts an inhibitory effect on collagen synthesis by antagonizing Smad3, a key effector in the transforming growth factor-beta (TGF-β) signalling pathway. TGF-β/Smad3 normally promotes collagen gene expression; however, AP-1 competes with or suppresses this activity, effectively downregulating collagen synthesis while simultaneously promoting matrix metalloproteinases (MMPs), which degrade existing collagen fibrils (Chung *et al.,* 1996; Quan *et al.,* 2002). When both AP-1 and Smad3 pathways are co-activated, the inhibitory effects of AP-1 dominate, leading to a net reduction in collagen production and an accumulation of fragmented ECM components (Fisher *et al.,* 2002; Fisher *et al.,* 2008). A visualisation of this phenomenon can be found in Figure 2. This visualisation shows the multifaceted pathways in which UVR contributes to collagen deterioration. The progressive deterioration of collagen architecture and fibroblast function underscores collagen synthesis and preservation as a central therapeutic target in the management of skin ageing (Uitto, 2008).

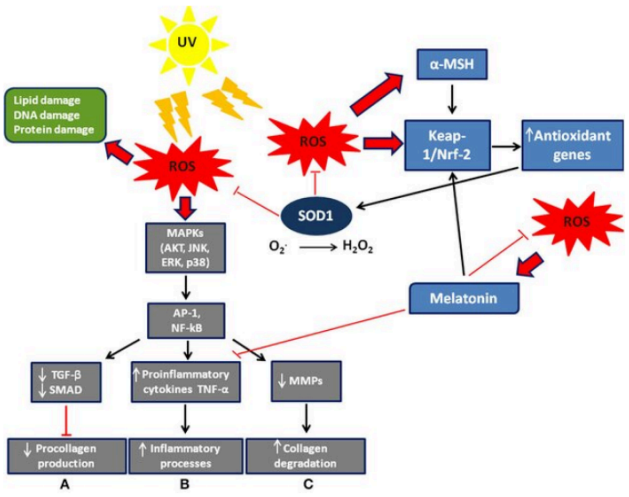


Figure 2: Scheme of ROS signaling/effects and defense system in the skin. Exogenous and endogenous agents of skin cells generate ROS, whose excessive levels can cause cell damage. ROS modulate MAP signaling pathways leading to activation of the transcription factor AP-1 (activator protein 1) and NF-kB (nuclear factor kappa-light-chain-enhancer of activated B cells). They also induce: (A) a decrease in procollagen synthesis via blocking TGF-β/SMAD signaling; (B) an increase in the inflammatory processes; (C) an increase in collagen degradation via synthesis of matrix degenerating MMPs. Furthermore, ROS allow nuclear factor Nrf2 to detach from its cytoplasmic inhibitor, keap-1, to translocate to the nucleus and activate transcription of antioxidant genes. Melatonin and α-MSH are also stimulated by ROS to activate Nrf2 dependent-pathways and then the expression of antioxidant genes. The Nrf2 pathway is activated not only in different skin cells such as keratinocytes and melanocytes, but also in fibroblasts. Modified by Sardy. (Source: Altobelli *et al.,* 2020).

ii. Elastin Destruction

Elastic fibres are indispensable components of the dermal ECM, playing a central role in maintaining the skin's elasticity, recoil capacity, and structural resilience. Synthesized primarily by fibroblasts, these fibres are composed of a core of elastin surrounded by microfibrillar proteins, including fibrillin and other glycoproteins, which provide the scaffolding necessary for proper elastin assembly (Gray *et al*., 1973; Kielty *et al.,* 2002; Mecham, 1991). Together, these elements form a highly organized fibrous network that imparts the characteristic “bounce-back” quality seen in youthful skin.

The biosynthesis and assembly of elastin is a complex, multi-stage process. Elastin is encoded by a single gene and is initially produced in the form of tropoelastin, a soluble polypeptide precursor synthesized in the rough endoplasmic reticulum of fibroblasts. Tropoelastin undergoes intracellular post-translational modifications and associates with elastin-binding proteins before being secreted into the ECM (Weihermann *et al.,* 2016). In the extracellular environment, lysyl oxidase, a copper-dependent enzyme, catalyses the oxidative deamination of lysine residues, enabling the covalent cross-linking of tropoelastin monomers into mature, insoluble elastin fibres. This assembly occurs along a scaffold of microfibrils, particularly those rich in fibrillin, which guide and align the deposition of tropoelastin monomers into structurally coherent fibres (Sakai *et al.,* 1986; Zhang *et al.,* 1994). Reference Figure 3 for a visualisation of the elastin synthesis process within a simplified cellular environment. Disruptions in the synthesis, processing, or assembly of elastic fibres can lead to connective tissue disorders and manifest visibly in cutaneous ageing.

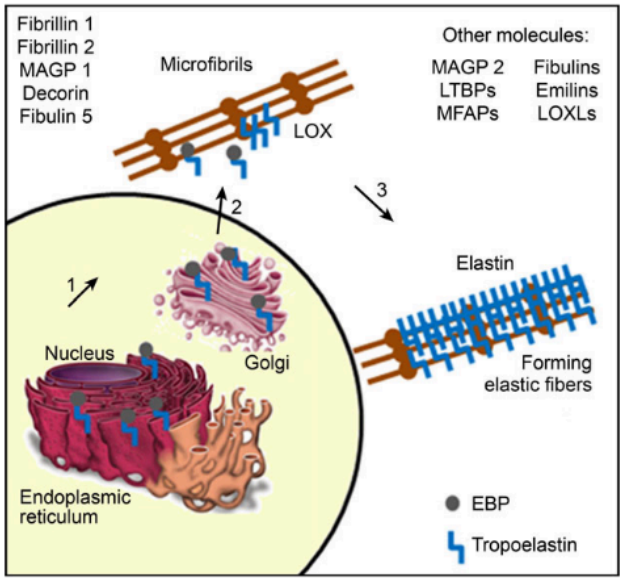


Figure 3: The elastogenesis first step (1) occurs inside the nucleus where the proteins formation is located in the endoplasmic reticulum. The Golgi complex stores and transports these proteins to the extracellular matrix where there is the formation of elastic fibres. During this phase, the elastin-binding proteins (EBP) associate with tropoelastin monomers to become a complex form before being released on the cell surface (2). During the formation of elastic fibres, microfibrils components function as a scaffold where elastin will deposit and several other molecules are involved in the process, such as LOX, fibrillin, MAGPs, decorin, fibulins, among others. The mature elastin (3) is then formed by cross-linking of lysine and tropoelastin mediated by enzyme lysyl oxidase. (Source: Weihermann *et al.,* 2016).

Unlike collagen, which can be replenished to some extent in adulthood, elastin is produced in significant quantities primarily during early development and is rarely regenerated thereafter.

Consequently, elastin degradation leads to irreversible structural deterioration in the dermis (Weihermann *et al.,* 2016). This manifests during ageing when the regenerative capacity of fibroblasts declines, and the balance between elastin synthesis and degradation shifts unfavourably. Age-associated changes include reduced expression of lysyl oxidase and increased activity of neutrophils and macrophages, which contribute to the enzymatic degradation of mature elastin fibres (Godeau & Hornebeck, 1988; Rijken & Bruijnzeel, 2009; Werb *et al.,* 1982).

Among the most pronounced accelerators of elastin degradation is UVR. Chronic UVR exposure impairs the synthesis and integrity of elastic fibres, inducing a condition known as solar elastosis. This pathological hallmark of photoaged skin is characterized by the accumulation of disorganized, non-functional elastin aggregates within the dermis, replacing the finely structured elastic network found in youthful skin (Pasquali-Ronchetti & Baccarani-Contri, 1997; Uitto, 2008). Solar elastosis results from a cycle of repeated elastic fibre damage, incomplete ECM remodelling, and the deposition of aberrant elastin structures. Chen *et al.* (2009) suggests that alternative splicing of the elastin gene under UVR-induced stress may contribute to the synthesis of defective elastin, thereby exacerbating the deposition of dysfunctional fibres. Ultimately, this degradation of elastic fibres and the resulting loss of skin elasticity are critical contributors to the visible signs of ageing, including wrinkling, rough texture, and diminished firmness (Scharfetter-Kochanek *et al.,* 2000).

Current therapeutic strategies for restoring elastic fibre integrity remain limited. Preliminary research has explored plant-derived compounds such as dill extract (Cenizo *et al.,* 2006) and denatured soybean extract (Mao *et al.,* 2013), both of which have shown some promise in stimulating elastin-related pathways. However, the evidence remains inconclusive, and further studies are required to establish their clinical relevance and efficacy in reversing age-related declines in skin elasticity.

i. Extracellular Matrix Damage

Fibroblasts play a central role in maintaining dermal structure and function by synthesizing key components of the ECM, including collagen, elastin, and glycosaminoglycans. In youthful skin, fibroblasts are tightly anchored to a structurally coherent ECM, predominantly composed of Type I collagen, which provides both mechanical support and biochemical cues essential for cellular activity and survival (Cole *et al.,* 2018; Fisher *et al.,* 2008). This physical and functional interaction between fibroblasts and the ECM is integral to sustaining dermal homeostasis. However, with advancing age, the ECM undergoes progressive degradation and fragmentation, particularly of

collagen fibres, resulting in compromised fibroblast-ECM adhesion (Fisher *et al.,* 2008; Fisher *et al.,* 2009; Fisher *et al.,* 2015; Quan *et al.,* 2013; Varani *et al.,* 2006).

Because of diminished matrix integrity, fibroblasts exhibit morphological and functional alterations. Ageing fibroblasts adopt a shrunken, elongated, and collapsed morphology, indicative of cytoskeletal disorganization and reduced mechanical tension (Fisher *et al.,* 2015; Quan *et al.,* 2013). These morphological changes are not merely passive reflections of tissue degeneration but are hallmarks of cellular senescence and functional decline. The loss of anchorage and mechanical cues impairs the ability of fibroblasts to maintain adequate ECM synthesis, including collagen, elastic fibres, and hyaluronic acid, thereby accelerating dermal deterioration (Fayad *et al*., 2017; Quan *et al.,* 2013). This establishes a self-perpetuating cycle in which ECM degradation leads to fibroblast dysfunction, which in turn further reduces ECM production.

Central to the regulation of ECM homeostasis is TGF-β1, a cytokine that promotes collagen synthesis via the activation of Smad transcription factors (Chen *et al.,* 1999; Chen *et al.,* 2000; Ghosh *et al.,* 2000; Ignotz & Massagué, 1986; Raghow *et al.,* 1987; Quan *et al.,* 2010; Varga *et al.,* 1987). In youthful skin, TGF-β1 signalling maintains a dynamic balance between ECM production and degradation. However, age-related reductions in fibroblast size and cytoskeletal tension lead to the downregulation of TGF-β receptor II (TβRII), thereby attenuating TGF-β1 signalling and compromising ECM synthesis (Fisher *et al.,* 2015).

This attenuation is compounded by the activation of alternative pathways that promote matrix degradation. Notably, reduced fibroblast size and ECM integrity in aged skin appear to activate AP-1 enzymes responsible for ECM, collagen, and elastin breakdown (Qin *et al.,* 2017). The concurrent suppression of TGF-β1-mediated collagen production and AP-1-mediated enhancement of ECM degradation represent a critical molecular inflection point in the dermal ageing process. This dual mechanism not only depletes structural proteins but also impairs the biomechanical environment necessary for fibroblast functionality, further exacerbating senescence and tissue dysfunction. Thus, the degradation of the ECM is both a cause and consequence of fibroblast senescence and dysfunction. These interlinked processes underscore the complexity of dermal ageing, where impaired signalling, altered cell morphology, and disrupted matrix architecture collectively drive the visible and structural deterioration of skin.

ii. Skin Barrier Damage

The skin barrier, composed of the stratum corneum (SC), intercellular lipids, natural moisturizing factors, and the skin's resident microbiome, is fundamental to maintaining cutaneous homeostasis. It serves as the primary defence against environmental aggressors, pathogenic invasion, and transepidermal water loss (TEWL). However, with advancing age, this barrier undergoes structural and functional deterioration, reflecting broader physiological changes in the skin. The epidermis becomes thinner, largely due to keratinocyte atrophy, while the dermal–epidermal junction flattens as rete ridges diminish, see Figure 4 for a visualisation. These alterations collectively reduce the skin's mechanical stability and regenerative capacity (Kaya & Saurat, 2007; Kong *et al.,* 2015; Lee *et al.,* 2009; Schurer & Elias, 1991). These anatomical changes are closely associated with increased TEWL, which contributes to the characteristic dryness and fragility observed in aged skin (Waller & Maibach, 2005).

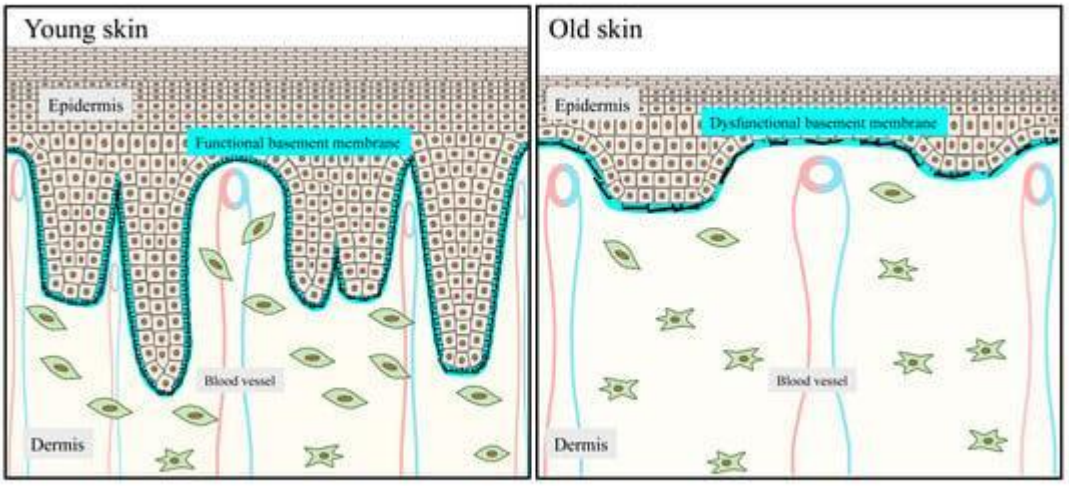


Figure 4: Visualisation comparison of rete ridge flattening. (Source: Roig-Rosello & Rousselle, 2020).

Ageing also compromises the molecular components critical to barrier function. Tight junctions, which ensure epidermal cohesion and paracellular impermeability, depend on integral membrane proteins such as claudin-1 and claudin-4. Age-related reductions in the expression of these proteins weaken the junctional integrity of the epidermis, further exacerbating permeability and vulnerability to external insults (Li *et al.,* 2019; Sugawara *et al.,* 2013). Simultaneously, the reduced number and function of keratinocytes impair lipid synthesis and SC cohesion, undermining the protective matrix that maintains barrier integrity (Farage *et al.,* 2008; Flament *et al.,* 2013; Ganceviciene *et al.,* 2012; Lee *et al.,* 2009).

Functionally, a robust skin barrier is essential not only for water retention but also for thermoregulation, immunological defence, and efficient wound healing (Barbieri *et al.,* 2014). When this barrier is compromised by age-related degeneration, it predisposes the skin to inflammation, delayed healing, and heightened susceptibility to irritants and allergens. Consequently, the incidence of dryness, pruritus, and contact dermatitis increases significantly with age (Berger & Steinhoff, 2011). Barrier-supportive topical interventions, particularly those formulated to restore lipids, maintain pH balance, and reinforce tight junction function, are thus vital not only in mitigating age-related skin dysfunctions but also in enhancing outcomes following dermatological and aesthetic procedures (Jourdan *et al.,* 2019).

iii. Glycation

Glycation is a non-enzymatic process wherein reducing sugars react with proteins, lipids, or nucleic acids to form advanced glycation end-products (AGEs). In the context of skin ageing, AGEs exert deleterious effects by promoting the cross-linking of collagen and elastin fibres. This cross-linking reduces fibre flexibility and mechanical integrity, directly impairing skin elasticity and contributing to the formation of wrinkles and sagging (Farage *et al.,* 2008). Importantly, glycation-induced damage operates independently of other ageing pathways such as UVR, environmental pollution, or intrinsic cellular senescence, thereby representing a distinct and compounding mechanism of dermal degradation (Rijken *et al.,* 2007). Furthermore, AGEs contribute to chronic oxidative stress and low-grade inflammation, further amplifying ECM deterioration and accelerating phenotypic signs of skin ageing, exemplifying the need for intervention through actives like retinoids.

iv. MMPs, UVR, and Free Radicals

Among extrinsic factors, chronic UVR exposure is the most significant contributor to premature skin ageing, commonly referred to as photoaging (Finkel & Holbrook, 2000; Rastogi *et al.,* 2010). Unlike intrinsic ageing, which typically becomes apparent in the later decades of life, photoaging manifests earlier and more aggressively, presenting as deep wrinkles, dermal laxity, uneven pigmentation, and telangiectasias, damaged superficial blood vessels (Farris & Rendon, 2010; Fisher *et al.,* 1997). Additionally, UVR exposure leads to elastosis and the fragmentation of collagen fibrils, particularly types I, III, and VII (Kang *et al.,* 2001; Rijken & Bruijnzeel, 2009; Sherratt, 2013; Uitto, 2008).

Central to these processes is oxidative stress mediated by UVR-induced ROS, reactive oxygen species. These free radicals initiate lipid peroxidation, protein oxidation, and DNA strand

breaks, collectively compromising cellular function and genomic integrity (Fisher, 2008; Finkel & Holbrook, 2000). UVB, with its higher energy and shallower penetration, directly damages epidermal DNA and impairs repair mechanisms, elevating the risk of pigmentation abnormalities and carcinogenesis (Choi *et al.,* 2018; Fitsiou *et al.,* 2021; Ravanat *et al.,* 2001). Both UVA and UVB generate ROS that damage nucleotides, induce mutagenic lesions, and impair mitochondrial function, thereby reinforcing the molecular hallmarks of ageing (Cadet *et al.,* 2014; Rastogi *et al.,* 2010).

In addition to genotoxic effects, UVR stimulates pro-inflammatory signalling pathways and induces the upregulation of MMPs. MMP-1 (collagenase) initiates the cleavage of native collagen fibrils, while MMP-3 and MMP-9 further degrade gelatin, elastin, and other matrix components (Fisher *et al.,* 1997; Fisher *et al.,* 2002; Quan *et al.,* 2009). UVR-generated ROS activate the transcription factor AP-1, which not only increases MMP expression but also suppresses collagen synthesis via inhibition of TGF-β/Smad signalling (Fisher *et al.,* 1996; Fisher & Voorhees, 1998; Quan *et al.,* 2010). This dual effect, enhanced matrix degradation and inhibited renewal, drives a net loss of structural integrity in the dermis (Dubey *et al.,* 2009; Rittie & Fisher, 2002). In addition to collagen breakdown, elastin degradation is mediated by MMP-12, a protease secreted by keratinocytes, fibroblasts, and immune cells, which contributes to the accumulation of disorganized elastotic material characteristic of photodamaged skin (Chung *et al.,* 2002; Ryu *et al.,* 2014; Chen *et al.,* 2005). This process is clearly shown within Figure 5, which shows more specific mechanisms by which MMPs, ROS, and UVR damage impact collagen within the skin.

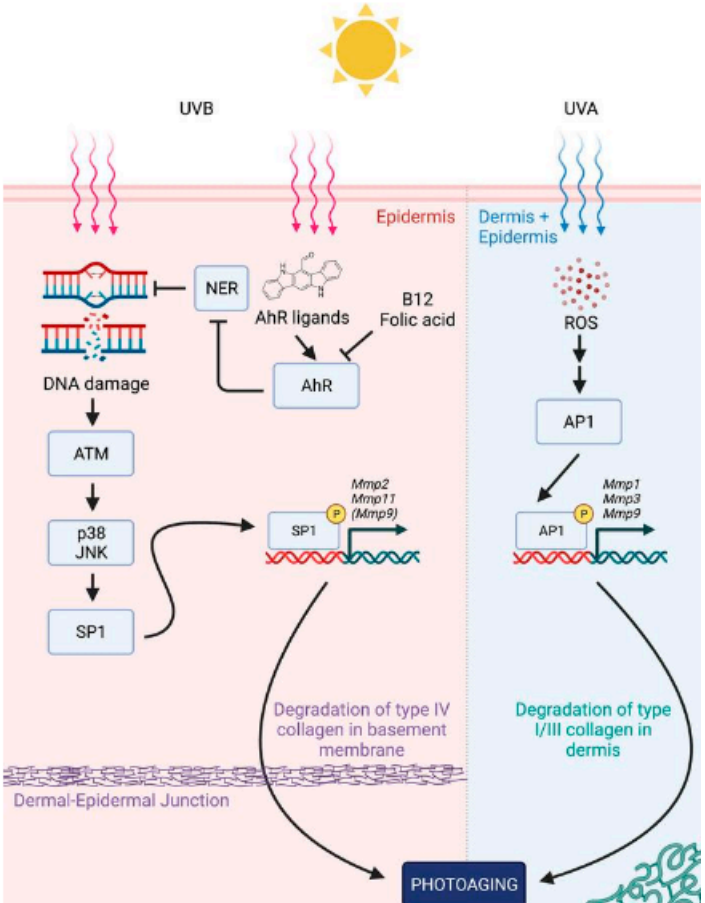


Figure 5: Proposed model for MMP induction in photoaging. (Source: Kim *et al.,* 2022).

v. Inflammation

Ageing is often characterised as chronic, low-grade inflammation, a phenomenon termed "inflammaging", which plays a key role in perpetuating ECM degradation, among other processes. Inflammaging is marked by elevated levels of pro-inflammatory cytokines and increased infiltration of immune cells such as eosinophils, mast cells, and mononuclear cells, which collectively amplify MMP activity and contribute to dermal breakdown (Quan *et al.,* 2013; Poon *et al.,* 2014). Concurrently, the number and functionality of epidermal Langerhans cells, a type of immune system cell, decline, compromising immune surveillance and the skin's ability to respond to environmental insults (Varani *et al.,* 2008).

This pro-inflammatory state is compounded by immunosenescence, the age-related deterioration of immune efficacy. Diminished T-cell responsiveness and reduced macrophage function impair wound healing, immune modulation, and tissue repair (Goldberg & Dixit, 2015). These immune deficiencies not only increase susceptibility to infections but also hinder the resolution of inflammation, leading to persistent tissue damage and a further decline in structural proteins such as collagen and elastin (Chen *et al.,* 2012; Weber & Niessen, 2012). Thus, the convergence of inflammageing and immunosenescence establishes a feedback loop that accelerates both visible ageing and functional deterioration of the skin barrier.

vi. Hyperpigmentation

Hyperpigmentation disorders, including solar lentigines (age spots), melasma, and post-inflammatory hyperpigmentation (PIH), are increasingly prevalent with age, particularly in chronically photoexposed skin (Cestari *et al.,* 2014; Sofen *et al.,* 2016). PIH is especially common in individuals with darker skin tones, where heightened melanin production in response to inflammation or trauma often leads to prolonged and recalcitrant pigmentation (Flament *et al.,* 2013). Despite a greater susceptibility to hyperpigmentation, individuals with higher melanin levels typically show delayed onset and reduced severity of photoaging, characterized by fewer wrinkles and diminished solar elastosis compared to lighter phototypes (Amici *et al.,* 2023; Chien *et al.,* 2018; Langton *et al.,* 2019). Nevertheless, histological analyses reveal that both lighter and darker

skin types share common markers of ageing, including epidermal thinning and flattening of the dermal–epidermal junction (Langton *et al.,* 2019).

Chronic UVR exposure is also implicated in the epigenetic regulation of melanogenesis. UVR can induce DNA methylation changes that upregulate pigment-producing pathways, contributing to age-associated pigmentation disorders (Campuzano-García *et al.,* 2019; Gilchrest, 1989; Yaar *et al.,* 2002). Solar lentigines, typically observed in fair-skinned individuals, are emblematic of cumulative UV exposure. Whereas melasma, which is often hormone-related, is more prevalent in darker skin types and exacerbated by genetic predisposition and heightened basal melanin synthesis (Bolognia *et al.,* 2012; Grimes, 1995). Emerging evidence suggests that melasma-associated hypermethylation may be reversible with topical agents such as niacinamide, sunscreen, and RA, highlighting potential epigenetic targets for intervention (Campuzano-García *et al.,* 2019).

Given the substantial psychosocial burden of pigmentation disorders, especially among individuals with richly pigmented skin, there is a pressing need for nuanced, evidence-based, and inclusive treatment approaches. Further research into the molecular, genetic, and epigenetic underpinnings of pigmentation will be critical in developing efficacious therapies tailored to diverse populations (Flament *et al.,* 2013; Grimes, 1995).

a. Ageing Summary

Skin ageing is driven by a network of interdependent biological mechanisms, in which the disruption of one pathway often amplifies others. Hormone changes and cellular and immunosenescence create an underlying system of ageing that is only exacerbated by outside factors. Extrinsic stressors, particularly UVR, trigger ROS overproduction, leading to oxidative damage of cellular lipids, proteins, and DNA. This oxidative stress not only directly degrades structural proteins but also activates AP-1 signalling cascades, which in turn upregulates MMP expression, accelerating collagen and elastin breakdown in the ECM. ECM degradation weakens dermal support, which impairs mechanotransduction in fibroblasts, further reducing collagen synthesis and promoting cellular senescence.

Simultaneously, dysregulated melanogenesis, driven by oxidative stress and chronic inflammation, produces uneven pigmentation and further oxidative burden through melanin-related ROS generation. Barrier impairment, resulting from disrupted keratinocyte differentiation and lipid synthesis, allows greater TEWL and increased penetration of environmental irritants, which fuels low-grade chronic inflammation. This inflammation sustains a cycle of oxidative stress, ECM degradation, and barrier weakening, creating a self-perpetuating loop that accelerates visible and functional ageing.

Retinoids remain the benchmark intervention for targeting multiple points in this cascade, including suppression of MMP expression, stimulation of fibroblast activity, normalisation of epidermal turnover, and partial restoration of barrier lipids. While retinoids are the current benchmarks of the anti-ageing industry, they don't function without fault. Understanding their mechanisms, downfalls, and implementation helps to identify gaps in research, holistic sustainability, and consumer needs.

I. Retinoids

a. Retinoids Overview

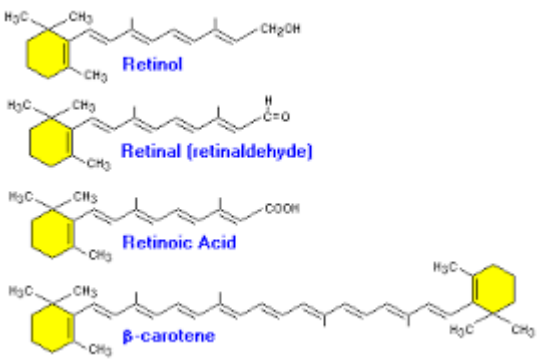


Figure 6: Vitamin A and related molecules. (Source: Knight *et al.,* 2024).

Retinoids represent a class of lipophilic compounds structurally derived from vitamin A, composed of four isoprene units arranged in a head-to-tail configuration, a conjugated polyene side chain, and a β-ionone ring (Harrison, 2012; Nomenclature of Retinoids, 1982). The structural configuration allows these molecules to participate in redox reactions, serve as transcriptional regulators, and integrate into lipid-rich cellular environments. Whether endogenously produced or synthetically derived, retinoids exert their biological functions predominantly through ligand-dependent activation of nuclear receptors, modulating gene transcription either directly or following intracellular metabolic conversion (Vivat-Hannah & Zusi, 2005).

Functionally, retinoids may exist as alcohols (retinol), aldehydes (retinal), carboxylic acids (retinoic acid), or esters (retinyl esters), with each form displaying different potency, bioavailability, and receptor affinity. Based on structural evolution and receptor selectivity, retinoids are conventionally classified into three generations. The first generation includes non-aromatic, non-selective compounds such as retinol, tretinoin (all-trans retinoic acid; ATRA), and isotretinoin. The second generation introduces a monoaromatic ring, as seen in etretinate and acitretin. The third generation comprises polyaromatic structures like adapalene, tazarotene, and arotinoid, designed for greater receptor selectivity and reduced systemic toxicity (Khalil *et al.,* 2017). Figure 6 shows a variety of the commonly used retinoids, to exemplify their structural differences.

b. Mechanisms of Action

Retinoids elicit their effects via non-genomic and genomic pathways. Non-genomic mechanisms, while less explored in dermatological applications, involve rapid, transient modulation of intracellular signalling pathways. These include alterations in calcium influx, kinase activation, and cyclic adenosine monophosphate levels, which may contribute to early changes in cellular dynamics but are not the primary drivers of long-term skin remodelling (Tang & Gudas, 2011).

The predominant and therapeutically relevant actions of retinoids operate through genomic mechanisms mediated by nuclear hormone receptors. Specifically, retinoids bind to and activate retinoic acid (RA) receptors (RARα, RARβ, RARγ) and retinoid X receptors (RXRα, RXRβ, RXRγ),

which dimerize, typically as RAR/RXR pairs, and bind to RA response elements (RAREs) in the promoter regions of target genes (Kang *et al.,* 2020). Upon activation, this receptor complex regulates the transcription of over 500 genes implicated in keratinocyte proliferation, differentiation, apoptosis, immune response modulation, and ECM homeostasis (Bremner & Faresse, 2020).

a. Retinoid Benefits

i. Keratinisation

A central mechanism by which topical retinoids exert their dermatological effects is through the regulation of keratinization**,** the orchestrated process whereby basal keratinocytes proliferate, differentiate, and migrate upward through the epidermis, and ultimately form the SC. Retinoids enhance desquamation and epidermal renewal by modulating gene expression that governs keratinocyte differentiation, adhesion, and barrier function. One critical molecular target is filaggrin, a filament-aggregating protein essential for epidermal integrity, natural moisturizing factor production, and SC cohesion (Kafi *et al.,* 2007). The degradation or thinning of the SC observed in vitamin A deficiency, manifesting as xerosis and increased barrier permeability, underscores the indispensable role of retinoids in maintaining epidermal homeostasis (Irby *et al.,* 2008).

At the transcriptional level, retinoids influence keratinocyte behaviour in part through the AP-1 pathway, a dimeric transcription factor composed of c-Jun and c-Fos subunits. AP-1 is activated in response to various stimuli, including growth factors and cytokines, and plays a pivotal role in regulating genes involved in keratinocyte proliferation and terminal differentiation. In a study examining retinol-treated skin, increased epidermal c-Jun protein expression was observed in tandem with epidermal thickening, suggesting a direct mechanistic link between topical retinol application, AP-1 modulation, and structural enhancement of the epidermis (Shao *et al.,* 2016). This thickening not only contributes to improved skin texture and resilience but may also enhance sebaceous activity, attenuate the appearance of fine lines, and restore mechanical support to photoaged skin.

i. Collagen

Retinoids are central to dermal remodelling through their dual ability to stimulate the synthesis of structural ECM proteins while simultaneously inhibiting matrix degradation. At the molecular level, ATRA, the most biologically active retinoid, upregulates the transcription of procollagen types I and III, the predominant structural proteins in the dermis responsible for tensile strength and resilience (Varani *et al.,* 2000). Concurrently, ATRA suppresses the activity of MMPs**,**

specifically MMP-1 (collagenase), MMP-3 (stromelysin), and MMP-9 (gelatinase), which are enzymes that catalyse collagen breakdown and are significantly upregulated in photoaged skin (Fisher *et al.,* 1996). This mechanism is integral to retinoids' anti-ageing properties.

Retinoids also promote fibroblast activation**,** leading to increased synthesis of glycosaminoglycans**,** such as hyaluronic acid, which play critical roles in maintaining dermal hydration, volume, and viscoelasticity (Kafi *et al.,* 2007). These biological effects translate into clinically perceptible improvements in fine wrinkles, roughness, and dermal thickness, typically observed within 12–24 weeks of topical application, consolidating retinoids' position as the "gold standard" in anti-ageing skincare (Mukherjee *et al.,* 2006).

The pro-collagenogenic properties of retinoids have been robustly demonstrated across multiple experimental and clinical studies. Varani *et al.* (2000) reported that even a short 7-day course of topical retinol increased fibroblast numbers in aged, sun-protected skin, underscoring retinoids' rapid and potent biological activity. While the precise mechanisms remain incompletely defined**,** inhibition of MMP activity and activation of fibroblast function via the TGF-β signalling pathway have been identified as pivotal. This pathway enhances fibroblast proliferation and ECM protein expression, leading to increased production of immature and mature collagen (Quan *et al.,* 2010; Rossetti *et al.,* 2011).

Further mechanistic insight is provided by Li *et al.* (2017), who demonstrated that ATRA administration in photoaged mouse skin elevated collagen content and protected collagen fibres from UVR-induced degradation. These protective effects were mediated through RAR and RXR activation, leading to suppression of c-Jun (Li *et al.,* 2017; Gericke *et al.,* 2013). This suggests that retinoids not only stimulate collagen synthesis but also inhibit photodamage-mediated degradation, reinforcing their bifunctional role in ECM preservation.

The retinoid-induced upregulation of collagen IV and elastin, as reported by D'Arcangelis *et al.* (2024) during their clinical study of periorbital ageing, further supports their comprehensive impact on dermal architecture. Similarly, Qu *et al.* (2018) demonstrated that retinol enhances the expression of TGF-β and procollagen III, while suppressing miR-29a, a microRNA that negatively regulates collagen gene expression. The findings by Kong *et al.* (2015) corroborate this, showing increased gene and protein expression of COL1A1 and COL3A1, key mediators of dermal regeneration. Immunostaining studies by Shao *et al.* (2016) and Rossetti *et al.* (2011) confirmed

enhanced deposition of newer and mature collagen following retinol treatment, offering histological validation of these effects.

Importantly, Halai *et al.* (2024) provided crucial evidence that these retinoid mechanisms are conserved across diverse skin phototypes, including more melanated skin. In darker skin tones, retinoids were shown to elicit comparable effects on epidermal thickening, keratinocyte proliferation, and fibrillin-rich microfibril deposition at the dermal-epidermal junction, features essential for maintaining dermal elasticity and reducing visible signs of ageing.

The well documented affects of retinoids on dermal collagen remain clear. Across many different skin tones, different types of ageing, and different skin types, it remains a benchmark for many newer anti-ageing actives. While being a “gold standard”, this does not mean they are without fault, irritation or risk. This review continues to explore retinoids in a holistically sustainable way, in order to understand where issues are and where solutions or alternatives can be made to better suit the consumer and world.

ii. Elastin

Beyond their well-documented role in collagen synthesis, retinoids exert critical effects on elastin dynamics, particularly in the context of photodamage. Chronic UVR exposure leads to solar elastosis. Topical retinoids mitigate these changes by promoting the synthesis of new elastin and restructuring the ECM (Griffiths *et al.,* 2001). Mechanistically, RA modulates the expression of fibrillin and tropoelastin contributing to improved dermal resilience and restoring skin’s elastic recoil (Kang *et al.,* 2001). Histological analyses confirm that retinoid-treated skin exhibits superior elastic fibre organization and reduced elastotic material compared to untreated controls.

In a pivotal study, Rossetti *et al.* (2011) used ELISA to quantify elastin levels in human fibroblast cultures and demonstrated a significant increase following retinoid treatment. Notably, the study employed Luna staining, a method for visualizing elastic fibres, and observed an enhancement of the *in vitro* elastin network, substantiating the hypothesis that retinoids can directly induce elastin synthesis and fibre formation in human dermal fibroblasts. This marked the first clear evidence of such an effect in human cells.

Earlier, Tajima *et al.* (1997) explored similar mechanisms in embryonic chick fibroblasts, reporting that RA increased elastin synthesis. However, they concluded that RA alone did not significantly influence cell proliferation or elastin expression in the absence of metabolic activation,

highlighting the importance of retinoid oxidation and intracellular conversion for full biological efficacy. Preceding this, Schwartz and Kligman (1995) provided early evidence of retinoid-induced elastic fibre formation, showing an increase in tropoelastin in RA-treated hairless mouse skin via **i**mmunofluorescence, indicating the emergence of newly synthesized elastic tissue, and can be seen in Figure 5.

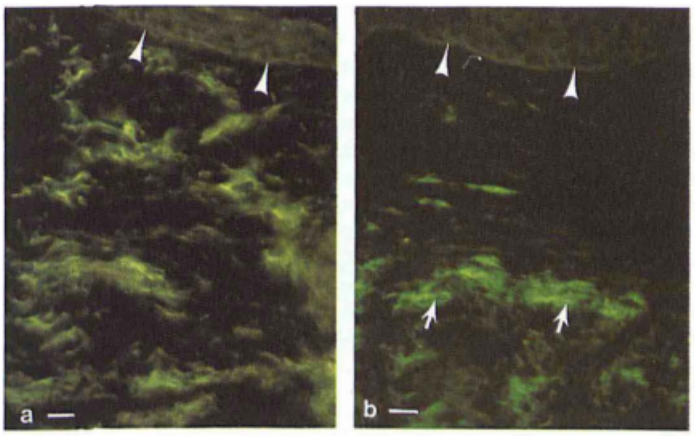


Figure 5: a) VVR for 10 weeks. Fluorescence is evident in diffuse thick and thin fibers throughout the dermis. *Arrowheads,* dermoepidermal junction. *Bar*, 10 μm. b) UVR. for 10 weeks followed by tretinoin for 10 weeks. An intensely stained band of elastosis delineates the lower border of the band of unstained new collagen (*arrows*). Within the dark band are thin fluorescent strands of elastin. *Arrowheads,* dermoepiderlllal junction. *Bar*, 10 μm. (Source: Schwartz & Kligman, 1995).

Building on this mechanistic foundation, Sołdacka *et al.* (2023) assessed clinical outcomes and reported modest but measurable improvements in skin elasticity parameters following retinol application, particularly in early-stage ageing**,** PIH**,** atrophic acne scarring, and enlarged pores. Although the improvements were not statistically significant in all cases, the study underscored retinoids' relevance in preventive and restorative skincare for compromised elastic integrity.

Collectively, these findings clarify that while retinoids cannot reverse elastin degradation, they can reactivate fibroblasts to support new elastin production, especially when introduced at the incipient stages of dermal ageing. This renewed elastogenesis may help preserve the skin's mechanical properties, particularly elastic recoil and tensile strength, which are hallmarks of youthful skin. Targeting early ECM disruption with retinoids offers a rational approach to attenuating visible skin ageing, and further underscores their role as mechanistically versatile and clinically validated topical agents.

iii. Extracellular Matrix

The ECM is foundational to skin architecture, supporting fibroblast function, collagen and elastin synthesis, and overall dermal integrity. As the primary structural component of the dermis, its maintenance is essential for resisting the degenerative changes associated with ageing. Connective tissue growth factors, particularly those regulated via the TGF-β pathway, are central to dermal remodelling and have been shown to be upregulated by retinoids, thereby contributing to enhanced ECM repair and regeneration (Quan *et al.,* 2010).

However, recent data introduced complexity to this model. Davis *et al.* (2024) reported a paradoxical downregulation of ECM-related structural gene expression in both clinical and *ex vivo* skin treated with ATRA and cosmetic retinoid formulations. The authors propose that this transient reduction may reflect an initial remodelling response like that observed following non-ablative fractional laser treatments, where early ECM suppression precedes a subsequent wave of collagen biosynthesis. This interpretation aligns with previous findings showing that peak collagen production occurs several months after retinoid application, suggesting that gene expression profiles may not immediately reflect long-term dermal outcomes.

In contrast, studies such as Shu *et al.* (2023) offer a more direct mechanism of ECM preservation. They demonstrated that multiple cosmetic retinoids, including retinol, retinyl palmitate, retinyl acetate, retinyl propionate, and hydroxypinacolone retinoate (HPR), inhibit MMPs, particularly MMP-9 across all tested compounds and MMP-3 (except in the case of HPR). As MMPs catalyse the degradation of ECM components their suppression by retinoids likely contributes to matrix preservation and resistance to photoageing.

Expanding on this, Han *et al.* (2025) focused on MMP-1, a primary enzyme implicated in UVB-induced collagen degradation. Using a patented microencapsulated spherulite-based retinol formulation, they demonstrated a significant reduction in MMP-1 expression post-UVB exposure. This dual action, suppressing enzymatic breakdown while simultaneously promoting collagen synthesis, reinforces the retinoids' role in ECM maintenance and highlights the potential of formulation technology in enhancing dermal outcomes.

Although topical retinoids do not interact directly with the ECM, their indirect modulation via fibroblast activation, MMP regulation, and photoprotection constitutes a powerful multi-mechanistic approach to preserving dermal structure. These findings collectively underscore the nuanced and temporally dynamic nature of retinoid-induced ECM remodelling and reinforce their central role in evidence-based anti-ageing dermatology (Quan *et al.,* 2010).

v. MMPs, UVR, and Free Radicals

Retinoids are well established as modulators of ECM homeostasis, primarily through their dual role in inhibiting MMPs and upregulating tissue inhibitors of metalloproteinases (TIMPs), both of which are central to ECM remodelling and preservation (Sorg *et al.,* 2006). TIMPs bind to active MMPs, neutralising their proteolytic activity and facilitating the repair and synthesis of structural proteins such as collagen and elastin. Most retinoid compounds exert their ECM-preserving effects by inducing the transcription of TIMP-encoding genes, which enhances the dermal microenvironment's resilience against enzymatic degradation. Notably, ATRA also exhibits a distinct mechanism of action: it directly suppresses MMP expression through inhibition of the AP-1, leading to downregulation of MMP-1, -2, -7, -9, and -13 (Zasada & Budzisz, 2019). Collectively, these mechanisms underpin retinoids' capacity to counteract both intrinsic and extrinsic ECM degradation, promoting sustained dermal regeneration and structural integrity.

ii. Hyperpigmentation

Hyperpigmentation is characterised by aberrant melanin production and distribution, driven by UV exposure, inflammation, hormonal dysregulation, and genetic predisposition. Retinoids exert depigmenting effects through several interrelated yet debated mechanisms. Traditionally, these agents have been understood to promote epidermal turnover, thereby accelerating the upward migration and desquamation of melanin-laden keratinocytes. This mechanical dispersal is complemented by biochemical effects, including the downregulation of tyrosinase gene transcription and disruption of melanin transfer from melanocytes to keratinocytes (Mukherjee *et al.,* 2006; Kafi *et al.,* 2007). However, emerging data suggest contention regarding the primacy of these mechanisms.

Tancrède-Bohin *et al. (*2020), using advanced visualisation technologies, questioned the conventional view that retinoids primarily inhibit melanogenesis at the transcriptional or enzymatic level. Their findings point instead to epidermal renewal and keratinocyte turnover as the predominant drivers of pigment correction. This introduces a critical distinction between the regulatory inhibition of melanin synthesis and the mechanical clearance of pigment, suggesting that retinoids may act more as modulators of epidermal kinetics than direct melanogenic suppressors. This contention underscores a need for greater mechanistic clarity, particularly given the implications for tailoring retinoid use across diverse skin phototypes and pigmentary disorders.

Clinical studies corroborate the efficacy of retinoids across a spectrum of hyperpigmentationdisorders. Kafi *et al.* (2007) demonstrated significant reductions in mottled pigmentation with retinol application, while Rafal *et al.* (1992) found ATRA to effectively lighten solar lentigines. Sołdacka *et al.* (2023) reported marked improvements in pigmentation and skin quality in lighter, Fitzpatrick I–III, skin using a 4% retinol formulation containing novel TGF-β activators and antioxidants, particularly among mature individuals with early signs of photoageing. However, this research leaves out many skin tone types, ultimately reducing the viability for use within the market towards people of colour.

Importantly, the pigmentary response to retinoids may be phototype-dependent. Bulengo-Ransby *et al.* (1993) conducted one of the few early studies on retinoid-induced pigmentary changes in Black patients. Over 40 weeks of ATRA use, PIH lesions significantly lightened, with the most pronounced changes occurring in the first month. Crucially, surrounding normal skin was minimally affected, indicating a relatively selective action on hyperpigmented lesions, which is an essential consideration for individuals with skin of colour.

Despite these benefits, the irritant potential of retinoids introduces clinical challenges. Paradoxically, inflammation induced by retinoids may transiently worsen pigmentation, particularly in more melanated skin prone to PIH. This underscores the necessity of cautious titration and, in many cases, the concurrent use of anti-inflammatory agents to mitigate irritation-related pigment rebound.

Ultimately, while the efficacy of retinoids in hyperpigmentation is well supported, the precise hierarchy of their mechanisms remains a subject of debate. This mechanistic ambiguity invites further investigation, particularly in the context of personalised dermatologic regimens tailored by phototype, pigment depth, and inflammatory risk.

b. Retinoid Issues

i. Skin Barrier Damage

Topical retinoids are well established to transiently impair the epidermal barrier, particularly during the initial phase of treatment. This disruption is marked by increased TEWL, reduced SC cohesion, and heightened sensitivity to external irritants (Barrachina *et al.,* 2022). These effects are both concentration- and vehicle-dependent and are most pronounced with prescription-strength agents such as ATRA. Nonetheless, with sustained use, compensatory adaptation occurs. Ultimately, retinoids normalize keratinocyte differentiation, increase epidermal

thickness, and restore barrier function, reflecting a biphasic response to treatment (Kang *et al.,* 2001).

Histological evidence supports this regenerative trajectory. Kong *et al.* (2015) reported epidermal thickening and rete ridge restoration following application of retinol and RA, associated with increased mitotic activity in basal keratinocytes, a mechanism also confirmed by Szymański *et al.* (2020). This proliferative effect enhances SC structure, contributing to improved barrier resilience over time. Additionally, Lee *et al.* (2020) demonstrated that a synthetic retinoid accelerated keratinocyte migration, thereby promoting wound healing and barrier repair. Newer formulations, such as HPR and encapsulated retinols, show promise in minimizing early barrier disruption. For instance, Davis *et al.* (2024) found that a 0.3% encapsulated retinol not only preserved barrier function, but also upregulated genes related to hydration and lipid synthesis.

However, not all studies portray retinoids as unequivocally beneficial to barrier integrity. Several mechanistic investigations reveal that ATRA may impair essential components of the epidermal architecture. Lee *et al.* (2009) found that RA suppresses the expression of key transcription factors involved in keratinocyte differentiation, thereby potentially destabilizing epidermal homeostasis. Bouwstra *et al.* (1995) had earlier established that keratinocyte-derived lipids are critical for SC cohesion and overall barrier function, highlighting the importance of lipid metabolism in epidermal integrity.

Further, Li *et al.* (2019) employed transcriptomic analysis of ATRA-treated HaCaT cells to reveal widespread dysregulation of genes involved in adherens junctions, tight junctions, and focal adhesion complexes. Notably, ATRA disrupted the expression of the epidermal differentiation complex, including filaggrin and small proline-rich proteins, essential for cornified envelope formation. Additionally, numerous keratins and keratin-associated proteins were dysregulated, suggesting impaired terminal differentiation. Importantly, ATRA modulated lipid metabolism-related genes, indicating an increased rate of lipid catabolism that may deplete protective lipids necessary for barrier integrity. Claudin expression was also altered, with reduced claudin-1 and increased claudin-4, signifying perturbations in tight junction homeostasis that could undermine intercellular cohesion.

These molecular alterations may underpin the clinical manifestations often observed in early retinoid use, such as dryness, roughness, irritation, and inflammation (Ale *et al.,* 1997). While epidermal adaptation can restore homeostasis over time, these findings underscore the need to

balance therapeutic efficacy with tolerability, particularly in sensitive skin phenotypes. Formulation strategies, including lower concentrations, emollient co-formulation, and slow-release delivery systems, remain essential to minimizing barrier disruption while preserving clinical benefit.

ii. Glycation

Glycation is a non-enzymatic process in which reducing sugars react with proteins, leading to the formation of AGEs. These compounds accumulate in the dermis, promoting collagen crosslinking, dermal stiffness, reduced elasticity, and a characteristic yellowish skin tone. This process is markedly accelerated by UVR and oxidative stress, both of which intensify AGEs formation and the associated structural degradation.

Retinoids mitigate glycation-related skin ageing through several indirect mechanisms. By stimulating fibroblast activity, enhancing collagen synthesis, and promoting ECM turnover, retinoids facilitate the replacement of glycated, dysfunctional collagen with newly synthesized, functional matrix components (Callaghan *et al.,* 2021). Additionally, emerging evidence suggests that retinoids may inhibit the expression of the receptor for AGEs (RAGE), thereby reducing downstream pro-inflammatory signalling and limiting cumulative dermal damage. While the anti-glycation properties of retinoids are less well-characterized than their effects on ECM remodelling or pigmentation, their ability to support dermal regeneration positions them as adjunctive agents in mitigating glycation-associated skin ageing.

However, this protective role is not without contention. Gelain *et al.* (2011) demonstrated that under specific conditions, particularly in ageing or stressed skin, retinol may paradoxically act as a pro-oxidant. Their study showed that retinol increases ROS production, which activates stress-responsive signalling cascades such as p38 MAPK and Akt. The p38 pathway, triggered by oxidative stress, regulates genes involved in inflammation and apoptosis, while Akt activation was linked to upregulation of RAGE expression. These molecular events may promote both AGE accumulation and DNA damage, contributing to compromised skin integrity, increased wrinkle formation, and impaired cellular repair.

Although glycation may represent a less dominant mechanism in the overall landscape of skin ageing, its interaction with oxidative stress and retinoid-induced signalling underscores the need for a nuanced understanding of retinoid activity. Retinoids may simultaneously support dermal regeneration while exacerbating oxidative damage and pro-glycation signalling under certain conditions. This duality highlights the importance of formulation, dosing, and individual skin

physiology in retinoid therapy and signals a clear need for further research into their context-dependent effects on glycation and photoageing (Gelain *et al.,* 2011).

iii. Inflammation

Retinoids exhibit a paradoxical relationship with inflammation, demonstrating both pro-inflammatory and anti-inflammatory properties depending on context, concentration, and delivery method. In the early phases of use, they frequently induce irritation characterised by erythema, scaling, and increased sensitivity, collectively termed "retinoid dermatitis." These symptoms primarily result from barrier disruption and inflammatory activation. However, retinoids also exert significant anti-inflammatory effects through modulation of gene expression in keratinocytes and immune cells. ATRA downregulates pro-inflammatory cytokines such as IL-6, IL-8, and TNF-α, while suppressing AP-1 transcription factor activity, thereby reducing both inflammatory and MMP-mediated degradation processes (Fisher *et al.,* 1996). These actions underpin the clinical utility of retinoids in inflammatory dermatoses such as acne, rosacea, and photoageing. Moreover, Shu *et al.* (2023) reported that less irritating cosmetic retinoids, including retinyl esters and HPR, significantly suppressed cytokine expression in UVB-exposed keratinocytes, suggesting potential benefit in sensitive or inflammation-prone skin types.

Mechanistically, retinoid-induced irritation is thought to arise through three main pathways. First, receptor-mediated activity, particularly through RARγ, has been implicated in irritation. Chen *et al.* (1995) observed that non-selective retinoid activation of RAR subtypes can provoke cutaneous inflammation in rhino mouse and rabbit skin models. The lack of receptor specificity in many conventional formulations likely contributes to unnecessary gene activation and skin reactivity, although more targeted subtype-selective formulations remain underdeveloped (David *et al.,* 1988; Kim *et al.,* 2008). Second, RA has been shown to activate immune pathways by stimulating mast cells via RARα, thereby inducing pro-inflammatory mediator release (Babina *et al.,* 2015). This immune activation is sustained through feedback loops involving further cytokine expression and amplification of inflammatory signalling, as corroborated by Mukherjee *et al.* (2006). Third, Steinhoff *et al.* (2003) proposed a neurogenic mechanism wherein retinoids increase the excitability of nociceptors. In this model, retinoid-treated keratinocytes, melanocytes, and fibroblasts release cytokines that activate peripheral sensory neurons, producing hypersensitivity and neurogenic inflammation.

In addition, retinoid-induced disruption of the epidermal barrier significantly contributes to irritation. RA alters gene expression involved in the formation of tight junctions, lipid metabolism,

and the cornified envelope, thereby impairing barrier integrity (Li *et al.,* 2019). As discussed in prior sections, this disruption compromises SC cohesion and lipid-mediated protection, exacerbating TEWL and inflammatory susceptibility (Ale *et al.,* 1997). These changes may intensify the very skin ageing processes that retinoids aim to mitigate, including impaired wound healing, cellular senescence, and barrier breakdown.

Various strategies have been proposed to reduce irritation without compromising efficacy. Delivery technologies such as microsponges, liposomes, and encapsulation systems aim to stabilise the retinoid molecule and modulate its release. These approaches enhance skin tolerance by reducing the concentration of free, bioactive retinoid available at the surface (Latter *et al.,* 2019; Meza *et al.,* 2021). Ye *et al.* (2023) demonstrated that a 0.1% encapsulated retinol formulation significantly reduced irritation while maintaining clinical activity and photostability. Despite these advances, hypersensitivity remains a concern. Retinoids activate TRPV1 channels, which sensitise cutaneous neurons and increase responsiveness to subsequent stimuli, particularly UVR (Yin *et al.,* 2013). This hypersensitisation not only heightens discomfort but may also limit the safe use of other actives or environmental exposures in retinoid-treated skin.

Given the persistent challenges surrounding irritation, inflammation, and hypersensitivity, mitigation strategies remain essential to patient and consumer tolerability. While novel formulation technologies show promise, these limitations underscore the need for continued research into receptor-selective, barrier-compatible retinoids, or viable botanical alternatives with comparable efficacy but improved tolerability. Such alternatives may offer a more sustainable path forward in anti-ageing dermatology.

iv. Photosensitivity & Instability

Photostability remains a pivotal factor in determining the efficacy and safety of topical retinoid formulations. Traditional retinoids are highly photosensitive and rapidly degrade upon exposure to UVR, leading not only to diminished clinical efficacy but also to the formation of potentially irritant byproducts (Panchal *et al.,* 2023; Temova Rakuša *et al.,* 2020). Consequently, their application is typically limited to nighttime use unless stabilised formulations are employed.

Cosmetic retinoids vary widely in photostability and potency. ATRA precursors and retinol derivatives are often selected for over-the-counter (OTC) formulations due to improved tolerance and relative stability (Fluhr *et al.,* 1999). Retinyl esters, such as retinyl palmitate, demonstrate greater photostability but reduced bioactivity. Conversely, newer compounds like HPR offer enhanced stability and receptor-binding capacity, though they may not achieve the therapeutic potency of prescription-grade retinoids (Shu *et al.,* 2023). This trade-off underscores the need for improved formulation strategies that preserve efficacy without compromising stability or tolerability.

From a physicochemical perspective, retinoids are inherently unstable in aqueous or polar environments, which are common in cream and serum formulations, necessitating intracellular stabilisation via specific retinoid-binding proteins (RBPs). These include cellular retinol-binding proteins (CRBPs), cellular RA-binding proteins (CRABPs), and serum transporters like RBP3 and RBP4, which facilitate retinoid delivery and retention within keratinocytes (Khalil *et al.,* 2017). Despite these endogenous buffering mechanisms, external instability remains a considerable barrier.

Retinoids are particularly vulnerable to degradation by light, oxygen, and temperature. UVA radiation accelerates oxidative degradation, especially in the presence of atmospheric oxygen (Failloux *et al.,* 2004). Their characteristic polyene chain, comprising multiple conjugated double bonds, renders them highly susceptible to oxidative cleavage, isomerisation, hydrolysis, and fragmentation when exposed to light, heat, strong acids, or peroxides (Chen *et al.,* 2023). Even trace amounts of acid can disrupt the polyene structure, reducing bioactivity through molecular deactivation, a process especially detrimental to clinical performance (Lee et al., 2002).

The extent of this instability has been rigorously quantified. Temova Rakuša *et al.* (2020) assessed 12 commercial cosmetics containing 16 retinoid compounds. HPLC-UV analysis revealed that retinoid concentrations declined by 0–80% during six months of long-term storage at 25 °C, and by 40–100% under accelerated conditions at 40 °C. Photodegradation proved even more pronounced than thermal degradation, confirming light exposure as the principal factor affecting product integrity.

To address these vulnerabilities, advanced encapsulation technologies, such as microencapsulation, liposomes, and solid lipid nanoparticles, have emerged as effective delivery systems. These approaches protect retinoids from environmental stressors, improve dermal penetration, and reduce irritation potential (Latter *et al.,* 2019; Meza *et al.,* 2021). In parallel,

packaging innovations, including airless pumps and opaque tubes, have extended product shelf-life by minimising oxygen and light exposure during storage and use (Farris, 2022). Zhong *et al.* (2024) further demonstrated that formulation adjustments aimed at limiting oxidation during filling and storage significantly enhance long-term stability.

The structural modification of retinoids also plays a crucial role in mitigating degradation. For instance, Han *et al.* (2025) reported that microcapsule composite formulations of retinol exhibited superior photostability and retained higher bioactivity compared to non-encapsulated counterparts. This is consistent with findings from Milosheska & Roškar (2022), who emphasised that photostability directly influences bioavailability, and by extension, therapeutic efficacy.

Taken together, these findings underscore the necessity of robust formulation and packaging strategies to preserve retinoid activity. Enhancing photostability is not merely a formulation challenge but a prerequisite for maintaining consistent therapeutic outcomes, especially in products intended for daytime application. While these innovations are groundbreaking for cosmetics and dermatology, they can be expensive, not sustainable, or still result in irritation as no solution is perfect. The continued need for sensitive skin alternatives, especially for those experiencing ageing and skin thinning provide encouragement for companies and researchers to study more sustainable, cost effective, and non-irritating options in commercial spaces.

v. Systemic Absorption & Safety

Topical retinoids are generally characterised by minimal systemic absorption, rendering them safe for long-term use in most individuals. However, systemic exposure is modulated by factors such as concentration, surface area of application, duration of use, and the condition of the skin barrier. Compromised skin may increase percutaneous absorption. Among cosmetic retinoids, retinyl esters demonstrate the lowest systemic activity due to their dependency on multi-step metabolic activation. In contrast, more bioavailable derivatives such as HPR may exhibit slightly higher systemic availability, although still within a minimal risk range. Despite this, the potential for systemic side effects, particularly teratogenicity, continues to warrant caution, especially in contexts such as pregnancy where even theoretical risks carry clinical weight.

The teratogenic risk of systemic retinoids is well-documented, with oral administration linked to retinoid embryopathy, a syndrome involving a wide spectrum of severe congenital anomalies, including craniofacial, cardiovascular, axial skeletal, renal, and central nervous system

malformations seen in infants, and even in utero (Kamm, 1982; Williams *et al.,* 2020). Although the precise molecular mechanism remains elusive, these effects are thought to result from dysregulation of retinoid-responsive genes critical for embryonic patterning and organogenesis. The risk is exacerbated by the pharmacokinetics of retinoids with their high lipophilicity permits accumulation in adipose tissue, prolonging systemic availability, and contributing to a long biological half-life. Retinoid levels have been detected months, and in some cases, years, after discontinuation, even impacting blood donation eligibility (Beckenbach *et al.,* 2015).

Despite these concerns, topical retinoid use during pregnancy remains understudied. A pivotal investigation by Panchaud *et al.* (2012) found no statistically significant differences in spontaneous abortions, major or minor congenital malformations, or features indicative of retinoid embryopathy when comparing pregnant women who used topical retinoids with a control group. However, elective termination rates were marginally higher in the exposed group (6% vs. 2%), though no termination was attributed to identified malformations. Notably, the study did not report the specific reasons for these terminations, leaving open the possibility that perceived risk, rather than clinical observation, may have influenced decision-making. Thus, while the findings are reassuring, the authors ultimately support continued avoidance of topical retinoids during pregnancy due to an unresolved risk–benefit ratio and lingering theoretical concerns.

Another dimension of systemic safety pertains to bone health, particularly in populations at elevated risk of osteoporosis, such as postmenopausal women who are often the primary demographic for anti-ageing treatments. Oestrogen deficiency accelerates bone resorption by altering the bone turnover cycle and suppressing osteoblast activity (Ji & Yu, 2015). Age-related decline in osteogenic function further compounds this risk (Khosla, 2012). Hypervitaminosis A, especially in the form of chronic excessive retinol intake, has been implicated in reduced bone mineral density and increased fracture risk (Rutkowski & Grzegorczyk, 2012). Promislow *et al.* (2002) observed an inverse association between oral retinol intake and bone mineral density, suggesting a potential osteopenic effect. While topical retinoids are unlikely to achieve systemic levels capable of compromising bone health, caution may be warranted in patients with existing osteoporosis or at high risk of skeletal fragility, given the additive potential of subclinical exposures over time.

In summary, while systemic absorption of topical retinoids is generally limited, critical safety considerations persist in sensitive populations, particularly pregnant women and individuals at risk of bone loss. These risks underscore the importance of formulation, dosing, and patient education

in cosmetic and clinical use, as well as the need for further long-term studies on systemic bioactivity in real-world use.

c. Retinoid Summary

This chapter has outlined why retinoids have remained a benchmark and “gold standard” for anti-ageing regimes in dermatology and in the cosmetic market. They are extremely effective at mitigating MMPs, certain inflammatory markers, UVR and ROS damage, and encouraging collagen and elastin synthesis, ECM homeostasis, keratinisation, among others. Although, retinoids’ flaws and harmful effects have also been noted. Everything from increased inflammation to systemic absorption which could be a small concern for the average consumer, could be detrimental to sensitive populations. While mitigations methods are being researched, they still don’t offer a holistically sustainable solution that incorporates the concerns of people of colour, climate activists, science-based consumers, and labour rights activists. Finding a newer alternative will not take away from current research, but rather elevate it.

VI. Holistic Sustainability

a. Consumer Behaviour & Market Research

In February 2020, the World Health Organization declared the outbreak of coronavirus disease 2019 (COVID-19), initiating one of the most globally disruptive public health crises in modern history. While previous epidemics such as Ebola, H1N1, and Zika garnered international concern, none permeated the infrastructure of affluent, industrialized societies as extensively as COVID-19. In response, entire nations entered lockdown or operated at minimal capacity, halting global supply chains and prompting an unprecedented collective standstill (Lee & Kwon, 2022).

This prolonged disruption fostered new patterns of consumer behaviour, shaped by isolation, uncertainty, and re-evaluation of personal and collective values. With more unstructured time and heightened health anxieties, many consumers turned to self-directed learning, particularly in beauty, wellness, and public health (Officer, 2023). The result was a more discerning and ingredient-literate consumer base, capable of interpreting scientific claims, assessing formulations, and questioning industry norms. Simultaneously, widespread dissatisfaction with institutional pandemic responses undermined public trust in regulatory bodies, including those governing health, nutrition, and cosmetic safety (Kapoor *et al.,* 2019). This scepticism catalysed a broader interrogation of brand integrity, transparency, and safety within the beauty industry (Lee & Kwon, 2022).

Although “clean” and “natural” beauty movements existed pre-pandemic, they were largely peripheral and driven by communities wary of synthetic ingredients and often disengaged from conventional science. The pandemic pushed these values into the mainstream, as uncertainty amplified interest in perceived purity, safety, and environmental stewardship. Consumer demand increased for minimalist ingredient lists, low-preservative formulations, ethically sourced raw materials, and “chemical-free” branding. However, this trend also triggered a parallel rise in misinformation. Lacking toxicological expertise, many consumers misinterpreted chemical nomenclature or misunderstood the dose-dependent nature of safety evaluations, often conflating synthetic with harmful (Delannoy *et al.,* 2023; Officer, 2023). This undermined science-based risk communication and created market environments where perception, rather than data, dictated product success.

The pandemic's sociocultural effects were particularly profound among children and adolescents. Deprived of in-person socialisation, many migrated to digital platforms, where beauty and wellness influencers became primary sources of identity formation. These creators frequently promote products and routines, including anti-ageing and skin-whitening treatments, without scientific oversight or age-appropriate framing. This content, often monetized and algorithmically amplified, exposed a vulnerable demographic to adult-centric beauty ideals, with unclear psychological consequences. Despite the severity of this issue, industry accountability remains limited. Many of these marketing practices violate internationally recognised ethical standards, such as the ICC Framework for Responsible Marketing Communication, particularly regarding the protection of minors from exploitative messaging (Madhumita & Ponnarasu, 2024).

Beyond misinformation and youth marketing, ethical consumption faces a subtler but persistent barrier: social resistance. In hyper-visual, socially comparative environments, ethical consumption becomes both a political and personal act. Zane *et al.* (2015) observed that individuals who do not engage in sustainable consumption often disparage those who do, perceiving their behaviour as a threat to their own self-concept. This dynamic, grounded in psychological self-preservation, undermines both the ethical consumer and the critic, reinforcing social norms that favour conformity over accountability. Such peer-based devaluation discourages pro-social behaviour, normalizes unsustainable practices, and perpetuates market inertia. Brands aiming to promote sustainability must address these socio-psychological dynamics alongside product innovation and messaging strategies.

In sum, COVID-19 catalysed a fundamental shift in beauty consumerism, marked by heightened scrutiny, ethical expectation, and scientific curiosity. However, these gains are accompanied by persistent misinformation, exploitative marketing to youth, social pushback against ethical behaviour, and a complex, often opaque sustainability landscape. As the industry responds, addressing social barriers, and reinforcing regulatory standards will be essential in ensuring that the post-pandemic consumer is empowered not only to care, but to act responsibly. This consumer mindset became integral to consumer purchase behaviour, particularly within the anti-ageing sphere, as more progressive ideals of ageing were integrated into wider scepticism of powerful regulatory and consumer-centred bodies. Retinoids became a particular subject of interest, as more people started using the science-backed actives, they noticed the irritating and damaging side effects and spoke out for better alternatives or mitigating agents. Although, the desire for “green” ingredients still prevailed. Thus, more research needed to be done into this sector in order to keep up with consumer demands.

b. Business Sustainability & Consumer Influence

Business sustainability, while not a novel concept, has gained renewed traction among investors, regulators, and industry leaders. The modern sustainability discourse centres on the multiple-bottom-line framework, encompassing economic, governmental, social, ethical, and environmental performance metrics. Traditionally, success was measured through financial outcomes alone. However, events such as the 2007–2009 global financial crisis exposed the dangers of prioritizing profit over ethics. The crisis, partly driven by unethical financial decisions across private and public sectors, underscored the need for more comprehensive sustainability models (Rezaee *et al.,* 2019a).

Historically, sustainability regulation has been sparse, with businesses relying on governmental directives to identify and mitigate ecological harms. Many companies ignored sustainability until consumer pressure made it financially relevant. This reflects both a capital-centric business ethos and widespread misinformation about sustainable practices. As neoliberal capitalism continues to shape global economies, the integration of sustainability will require substantial institutional reform. Both corporate and governmental stakeholders must respond to evolving consumer priorities with urgency and accountability (Huckle & Wals, 2015).

Increasingly, businesses are adopting holistic approaches that integrate sustainability into core operations and corporate culture. This shift from reactive compliance to proactive transformation focuses on long-term strategies that benefit not only shareholders but also

employees, communities, and the environment. Rather than viewing sustainability as an external obligation, forward-thinking companies are embedding it within their operational ethos to foster resilience and relevance (Rezaee *et al.,* 2019b).

Despite lingering scepticism, sustainability concerns have gained legitimacy, particularly regarding environmental impacts of supply chains, resource sourcing, and corporate conduct. The United Nations' 2030 Sustainable Development Goals, adopted in 2015 by all member states, present a global blueprint for shared prosperity and ecological stewardship. Although progress has been uneven across industries, the cosmetic sector exemplifies the challenges of harmonizing sustainable practices. Recent efforts emphasize ethical consumption and the reduction of overconsumption, positioning consumer behaviour as a critical driver of change (The 17 Goals | Sustainable Development, 2015).

To navigate this increasingly complex ethical landscape, tools such as sustainability calculators have emerged as practical interventions. These calculators enable consumers and manufacturers to quantitatively assess the environmental impact of ingredients, formulations, or products across multiple life cycle stages, including production, packaging, transportation, and disposal. As outlined by Bom *et al.* (2020), sustainability calculators can foster transparency by translating abstract environmental concepts, such as carbon footprint, water usage, and resource depletion, into digestible, user-oriented metrics. Moreover, they help manufacturers optimise supply chains, select lower-impact ingredients, and align their practices with environmental regulations and sustainability goals. Crucially, they highlight that when integrated into digital platforms or product labelling, such tools empower consumers to make more informed choices, shifting agency from the brand to the individual. This represents a critical step in transitioning sustainability from a passive brand attribute to an active component of consumer decision-making.

Rohini and Meppurath (2024) examined ethical consumption in a different way, through five dimensions: environmental concern, preference for organic products, fair trade alignment, animal welfare, and anti-consumption activism. They reviewed 123 articles spanning 2000–2024. Their findings advocate for broader methodological diversity, cross-cultural perspectives, and exploration of under-researched mediators such as emotion and identity. Importantly, they emphasized the role of consumer perceptions in shaping both ethical consumption and business communication strategies. In parallel, Shahzad *et al.* (2024) investigated how emotional engagement and corporate social responsibility (CSR) practices influence green consumption in Pakistan and China. Their findings revealed that CSR initiatives, spanning environmental,

community, and customer domains, fostered stronger ethical purchasing behaviours in both contexts, with China showing a slightly more robust response. These insights reinforce CSR's dual function of improving organizational sustainability while cultivating consumer trust.

To address these challenges, businesses must adopt context-specific yet ethically grounded sustainability practices. Tan *et al.* (2019) propose a valuable taxonomy of strategies applicable across sectors, including the implementation of ISO 22716:2007 guidelines to ensure traceability and minimise contamination in cosmetic manufacturing, the integration of sustainability objectives into corporate values, mission statements, performance evaluations, and incentive structures, and the development of robust knowledge dissemination systems to educate both internal stakeholders and external partners on sustainability principles. Additionally, sustainable supply chain design, emphasising ethical sourcing and the reduction of upstream and downstream environmental harm, plays a critical role, as do comprehensive lifecycle assessments that measure the environmental impact of products from raw material extraction through to disposal. Complementing these are waste and emissions management systems underpinned by circular economy principles, which aim to reduce, reuse, and recycle material flows. Together, these interconnected strategies offer a scalable, systems-level framework for improving sustainability outcomes while maintaining operational and economic viability.

Ultimately, the most profound transformation in sustainable business arises from a mindset shift. When companies begin to consider their societal, ecological, and ethical impact alongside financial outcomes, a more comprehensive understanding of the market and its future emerges. As Shahzad *et al.* (2024) demonstrate, emotionally resonant CSR initiatives aligned with ethical values can significantly influence consumer behaviour. Combined with the rise in consumer education and awareness, these changes have the potential to revolutionize not only individual firms but entire industries (Gu *et al.,* 2024; Shahzad *et al.,* 2024). Theses practices, while may be difficult to integrate, show promise within the larger market financially, within brand loyalty, brand trust, and an overall more truly sustainable business model.

iii. Bakuchiol

a. Bakuchiol Overview

Bakuchiol is a monoterpene phenol primarily derived from the seeds of *Psoralea corylifolia* (Babchi), a plant native to South and Southeast Asia, particularly India and China, where it has long held significance in traditional medicine (Mehra *et al.,* 2024; Nabi & Shrivastava, 2017). Although also present in other *Psoralea* species, commercial bakuchiol is most commonly sourced

from *P. corylifolia*, which is now considered endangered in some subtropical regions due to unsustainable harvesting practices (Nabi & Shrivastava, 2017). This raises important concerns about the ecological viability of “natural” alternatives within the booming anti-ageing sector, particularly as consumer demand often outpaces the establishment of robust sustainability frameworks.

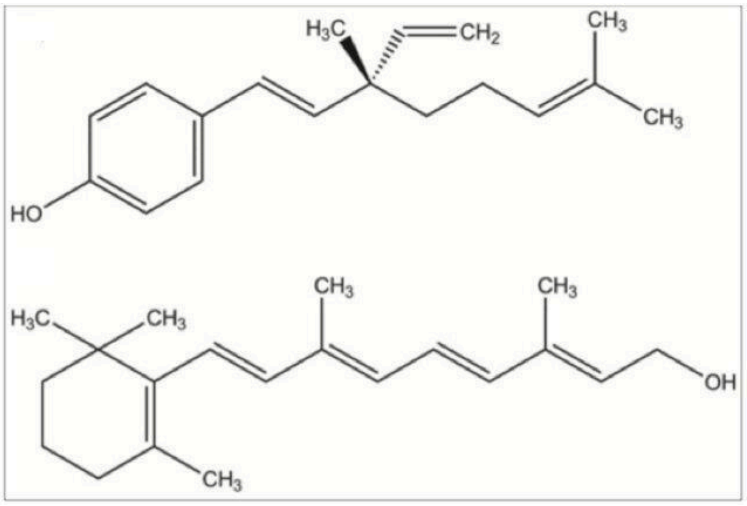


Figure 6: Chemical structures of bakuchiol (top) and retinol (bottom). Bakuchiol and retinol do not share structural similarity (Source: Park, 2022)

Bakuchiol’s positioning as a botanical retinoid alternative is driven largely by its phenotypic mimicry of retinoid effects, including antioxidant, anti-inflammatory, antibacterial, and anti-pigmentation actions (Ferrandiz *et al.,* 1996; Jafernik *et al.,* 2020; Kim *et al.,* 2016; Matsuda *et al.,* 2009; Polakova *et al.,* 2015). Though structurally distinct, see Figure 6 for a visual comparison of their structures, it lacks the polyene backbone and polar head group characteristic of retinoids, bakuchiol has been shown to modulate several of the same gene expression pathways implicated in ageing, pigmentation, and inflammation, such as downregulation of MMPs, suppression of pro-inflammatory cytokines (e.g., IL-6, TNF-α), and promotion of collagen synthesis (Chaudhuri & Bojanowski, 2014). Importantly, despite its hydrophobic nature, bakuchiol demonstrates high photostability and does not degrade easily under light or oxidative stress, contrasting favourably with the instability that often limits the topical use of retinoids. Nonetheless, its low water solubility requires careful formulation strategies to ensure optimal bioavailability and skin penetration, especially when included in emulsions or multi-phase systems (Adarsh Krishna *et al.,* 2022).

However, the narrative of bakuchiol as a “clean” or “green” substitute for retinoids often obscures the complex environmental realities of its production. While positioned as ethically superior, early extraction methods relied on solvent-based processes with ecological and safety

drawbacks. Addressing this, Lewińska *et al.* (2021) introduced a supercritical CO_2 extraction technique that significantly reduces chemical waste and preserves bioactivity, marking a critical advance in aligning ingredient sourcing with green chemistry principles. Similarly, Lystvan *et al.* (2009) demonstrated that other *Psoralea* species could be used to synthesise bakuchiol, offering a potential diversification of supply chains and reduced pressure on ecologically vulnerable populations.

Yet, despite these improvements, the anti-ageing market continues to commodify “natural” ingredients without always ensuring that their sourcing, extraction, or life cycle management meets holistic sustainability criteria. The use of bakuchiol exemplifies this paradox. It is simultaneously heralded as a plant-based, skin-compatible solution and implicated in the environmental degradation of native flora. This contradiction reflects broader tensions within the wellness and “clean” beauty sectors, where ethical narratives often mask unresolved sustainability gaps. As the market for botanical actives expands, there is a pressing need for regulatory and corporate mechanisms that account not only for product efficacy and consumer safety but also for biodiversity conservation, traceability, and long-term ecological impact.

Ultimately, bakuchiol’s popularity underscores the demand for multifunctional, non-irritating alternatives to conventional actives. However, its integration into sustainable skincare requires more than improved extraction technologies. It demands critical engagement with the socio-environmental costs embedded within the “natural” label. In this context, sustainability must be reframed as an intersectional process, one that spans agricultural practices, formulation science, consumer education, communal support and ethical marketing. The anti-ageing market, being so large, is the perfect sector to attempt to integrate this holistically sustainable mindset. The most change can be made, with the impacts being clearly visible, particularly in the context of retinoids as they have gained mass market popularity.

b. Retinoid Comparison

Bakuchiol, though relatively recent in its commercial adoption, has garnered significant attention within the anti-ageing sector due to its functional parallels with retinoids. While structurally distinct and operating via alternate signalling pathways, bakuchiol demonstrates comparable efficacy to retinoids in modulating key biological targets involved in skin ageing. Chaudhuri and Bojanowski (2014) identified that bakuchiol influences the expression of numerous

genes commonly associated with retinoid activity, including those governing retinoid binding and metabolism (RARB, RARG, CRBPs, CRABP1, LRAT), ECM integrity (collagen, elastin, fibronectin), dermal-epidermal junction stability, and hydration regulation (hyaluronate synthase, aquaporin channels). Notably, bakuchiol upregulates several of these genes to levels equal to or surpassing those induced by retinol, supporting its classification as a functional analogue with distinct yet overlapping mechanistic effects.

This molecular mimicry challenges the long-standing primacy of retinoids as the “gold standard” in anti-ageing skincare and underscores a critical shift in both consumer demand and scientific validation. The broader anti-ageing market, often driven by aggressive performance claims and synthetic actives, is increasingly scrutinised for its environmental footprint and long-term safety. In this context, bakuchiol’s plant-derived origin, favourable tolerability profile, and compatibility with holistic sustainability goals present a compelling alternative. However, the assumption that plant-based actives are inherently superior or more sustainable warrants caution. Sustainability claims must be supported by rigorous sourcing protocols and ecological impact assessments to avoid superficial “greenwashing.” As the market evolves, the success of alternatives like bakuchiol depends not only on efficacy but also on transparent, verifiable alignment with environmental and ethical principles.

i. Anti-Ageing

1. Collagen

The proliferative activity of retinoids underpins much of their clinically recognised anti-ageing efficacy, particularly through stimulation of collagen synthesis and ECM maintenance. Bakuchiol, though mechanistically distinct, elicits comparable biological responses. Bluemke *et al.* (2022) confirmed that bakuchiol promotes the expression of key ECM-related genes, notably COL1A1 and COL7A1, which encode type I and type VII collagen precursors respectively which are integral to maintaining dermal tensile strength and elasticity. Additionally, bakuchiol significantly upregulates fibronectin, a glycoprotein essential for cell adhesion and ECM stability. By supporting ECM architecture, bakuchiol mitigates structural degradation associated with deep wrinkle formation and skin laxity.

2. Antioxidant Behaviour

One of the principal mechanisms underpinning the efficacy of retinoids in anti-ageing interventions is their antioxidant activity. Bakuchiol demonstrates comparable, if not superior, antioxidant performance. Adhikari *et al.* (2003) elucidated the biochemical basis of bakuchiol’s

antioxidant function, attributing its enhanced efficacy to its structural features, particularly its terpenoid side chain. This chain provides readily abstractable hydrogen atoms that facilitate free radical scavenging. In addition, the molecule's phenolic bond possesses a high bond dissociation enthalpy, enabling efficient hydrogen donation to neutralise ROS. These molecular properties enable bakuchiol to exert robust antioxidant activity, surpassing that of retinol in free radical reactivity.

The importance of oxidative stress mitigation in anti-ageing biology is well established, as ROS accumulation accelerates dermal collagen degradation, ECM destabilisation, and cellular senescence. Bakuchiol's superior antioxidant capabilities thus hold significant implications for age-related dermal degeneration. Bluemke *et al.* (2022) support this by highlighting its wider efficacy across anti-ageing pathways, though the full extent of its therapeutic potential remains under-explored.

3. Inflammation

While retinoids are well-documented for inducing irritation and inflammation as part of their therapeutic profile, bakuchiol demonstrates a markedly different inflammatory response, one of active suppression. Bluemke *et al.* (2022) found that bakuchiol significantly reduced the levels of prostaglandin and macrophage migration inhibitory factor (MIF), both of which are elevated in response to chronic UVR and contribute to inflammatory signalling in skin. Notably, retinol failed to downregulate MIF expression in the same study. MIF plays a crucial role in skin ageing by upregulating MMP-1, the primary enzyme responsible for collagen breakdown. By inhibiting MIF, bakuchiol offers an upstream regulatory mechanism to suppress MMP-mediated degradation of the extracellular matrix, suggesting an anti-inflammatory and anti-ageing efficacy that may exceed that of retinoids (Bluemke *et al.,* 2022; Shimizu, 2005).

Beyond MIF, other inflammatory mediators contribute to age-related skin degeneration. Interleukin-8 (IL-8), a chemokine associated with mast cell and neutrophil infiltration in aged dermis, is a central marker of inflammation. Bacqueville *et al.* (2020) demonstrated that bakuchiol significantly suppressed IL-8 gene expression in UVR skin models, with levels nearly restored to those observed in non-irradiated controls. When combined with a vanillin-derived compound, the anti-inflammatory effect was synergistic, further reducing IL-8 and cellular senescence markers. One such marker, p16, a cyclin-dependent kinase inhibitor implicated in cellular ageing, was reduced by 44.4% with bakuchiol alone, nearly 7% more than the vanillin-based active, and even further when the two were used in tandem.

These findings underscore the unique mechanistic profile of bakuchiol. While retinoids target inflammation primarily through indirect modulation of cytokine expression and epidermal turnover, bakuchiol intervenes through alternative, complementary pathways, directly reducing proinflammatory chemokines, cytokines, and senescence markers. This distinction not only highlights its clinical relevance but also positions bakuchiol as a compelling anti-ageing agent for sensitive or inflammation-prone skin, one that offers high efficacy with reduced irritation risk.

4. Hyperpigmentation

The pigmentation-modulating effects of retinoids have been discussed previously in this review, particularly in the context of their proliferative and epidermal renewal functions. Bakuchiol demonstrates comparable depigmenting potential and may offer mechanistic complementarity. Herndon Jr. *et al.* (2016) reported that formulations combining bakuchiol with retinol enhanced depigmentation efficacy, suggesting a synergistic interaction between the two compounds. This aligns with bakuchiol's proposed action within the melanogenesis pathway, particularly its ability to modulate tyrosinase expression, the rate-limiting enzyme in melanin biosynthesis, and to interfere with Rho-dependent signalling, ultimately leading to reduced melanin production and pigmentation-related disorders (Kang *et al.,* 2020).

Sato *et al.* (2008) previously demonstrated that ATRA inhibits melanogenesis by suppressing tyrosinase activity, which historically formed the basis of understanding retinoid-based depigmentation. However, emerging evidence increasingly points to retinoids' indirect regulation of pigmentation through accelerated epidermal turnover and desquamation, thereby facilitating the removal of melanin-laden keratinocytes. This paradigm shift reframes the pigmentation pathway not as one governed solely by enzymatic suppression but as a secondary consequence of epidermal renewal and skin regeneration.

In contrast, bakuchiol appears to act more directly on melanogenic pathways while also providing proliferative support, allowing it to function through both mechanisms simultaneously. This dual approach enhances its value in pigmentation correction while potentially reducing the irritation often associated with retinoid-induced turnover. From a broader industry perspective, this reflects a significant evolution in the anti-ageing market. Signalling a movement away from monofunctional actives toward multi-mechanistic agents that deliver comparable or enhanced outcomes with greater tolerability.

ii. Anti-Acne

1. Sebum Alteration

Retinoids, particularly retinol, exert their anti-acne effects primarily through the modulation of sebum production. Crocco *et al.* (2021) demonstrated that retinoids reduce sebum synthesis by downregulating androgen signalling, specifically dihydrotestosterone (DHT), which binds to androgen receptors on sebocytes, influencing cell proliferation, differentiation, and lipid metabolism. Furthermore, retinoids inhibit key enzymes involved in lipogenesis further diminishing sebum output (Zasada & Budzisz, 2019). This dual mechanism not only regulates sebocyte activity but also contributes to the broader anti-inflammatory and anti-comedogenic actions attributed to retinoids in acne therapy.

Bakuchiol exhibits comparable efficacy in acne management through a multifaceted approach. Trompezinski *et al*. (2016) investigated the impact of bakuchiol on sebum composition in individuals with *Propionibacterium acnes* (now *Cutibacterium acnes*) colonisation and found that bakuchiol altered sebum profiles by increasing non-oxidised squalene and oleic acid, while reducing pro-inflammatory sapienic and linoleic acids. This compositional shift reflects a healthier, more stable sebum environment less conducive to acne pathogenesis. While elevated oleic acid may be associated with barrier impairment, this is a shared concern with retinoids, whose desquamative effects can similarly compromise barrier integrity.

Notably, bakuchiol's anti-acne efficacy extends beyond lipid modulation. It demonstrates direct antibacterial action against *C. acnes*, as well as potent antioxidant properties that mitigate lipid peroxidation, a key trigger in comedogenesis and inflammation (Trompezinski *et al.,* 2016). Additionally, its potential to influence 5-α-reductase activity, though not yet fully elucidated, suggests overlapping hormonal modulation pathways with retinoids, enhancing its therapeutic profile.

From a critical standpoint, bakuchiol's broader tolerability, lower irritation profile, and multifunctional properties position it as a compelling alternative in the acne treatment segment of the anti-ageing market. Its integration into skincare regimens not only addresses acne-related concerns but supports sustainable and plant-derived innovation.

2. Anti-Bacterial Activity

Bakuchiol demonstrates a distinct therapeutic advantage over retinoids in the management of acne, particularly through its direct antimicrobial activity, an area where retinoids are

comparatively limited. While acne vulgaris is multifactorial in origin, the proliferation of cutaneous microbes, particularly within the skin microbiota, plays a significant role in its pathogenesis. Targeting this pathway has become a key focus of cosmeceutical strategies.

Yin *et al.* (2004) established bakuchiol's significant antibacterial activity against *Staphylococcus aureus* and *S. epidermidis*, two common skin commensals that, when dysregulated, can contribute to inflammatory responses. Building on this, Trompezinski *et al.* (2016) demonstrated that bakuchiol is also effective against *Propionibacterium acnes* (now *Cutibacterium acnes*), a microorganism directly implicated in the development of acne lesions. Remarkably, bakuchiol exhibited comparable antibacterial efficacy to conventional topical agents such as benzoyl peroxide and zinc gluconate, cornerstones in current acne management (Trompezinski *et al.,* 2016; Yin *et al.,* 2004).

Moreover, bakuchiol's antifungal properties further differentiate it from retinoids. It has demonstrated activity against *Candida guilliermondii*, a pathogen frequently associated with superficial dermal infections (Pfaller *et al.,* 2006), and *Trichophyton mentagrophytes*, a dermatophyte implicated in tinea pedis (athlete's foot) (Ilkit & Durdu, 2014). Mechanistically, bakuchiol exerts its antifungal effects by increasing fungal membrane permeability and enhancing intracellular ROS generation, thereby inducing oxidative stress and compromising fungal viability (Lau *et al.,* 2014).

These multifaceted antimicrobial actions, both antibacterial and antifungal, underscore bakuchiol's unique positioning in skincare. While retinoids primarily address acne through sebocyte modulation and comedolytic effects, they lack intrinsic antimicrobial activity, often necessitating combination therapies. In contrast, bakuchiol offers an integrated solution, reducing microbial burden while simultaneously modulating inflammation, sebum composition, and oxidative stress.

iii. Concentration Regulations

Unlike retinoids, which are frequently associated with irritation, bakuchiol has demonstrated a more favourable tolerability profile. According to the European Chemicals Agency (*ECHA*, 2022), patch testing of bakuchiol did not yield sufficient evidence to classify it as an irritant or corrosive. However, it remains important to acknowledge that, like most topical actives, bakuchiol retains some potential for irritation depending on concentration and formulation. In contrast, regulatory frameworks around retinoid usage are significantly more restrictive. Under current EU regulation, leave-on cosmetic products containing retinoids are limited to a maximum concentration of 0.3%

(Commission Regulation (EU), 2024). While this threshold is grounded in extensive toxicological assessment, such generalised restrictions fail to account for the pharmacodynamic diversity of individual retinoid compounds or their nuanced mechanistic pathways. This one-size-fits-all regulatory approach narrows the scope of cosmetic innovation, particularly for dermatological concerns such as acne, photoaging, and psoriasis, conditions that often benefit from tailored retinoid concentrations or derivatives.

Moreover, the regulatory burden placed on retinoids has inadvertently constrained their widespread cosmetic application, resulting in a limited portfolio of commercially available retinoid-based cosmetics. This constraint continues to shape the direction of research, which remains largely fixated on optimising existing retinoids rather than broadening the paradigm of cosmetic actives. In contrast, bakuchiol, despite emerging as a potent bioactive with demonstrable efficacy across antioxidant, anti-inflammatory, antimicrobial, and collagen-stimulatory pathways, has received comparatively limited academic attention, particularly when not in direct comparison to retinoids. Yet, its mechanistic versatility and lower irritancy profile underscore its potential to not only match but, in some domains, exceed the performance of retinoids.

Critically, the prevailing research ethos in the anti-ageing space often reinforces existing hierarchies of active ingredients, privileging retinoids as the “gold standard” without fully interrogating alternative or complementary actives like bakuchiol. A more expansive and ecologically conscious research agenda, one that prioritises plant-based, holistically sustainably sourced, and biocompatible actives, could shift the future trajectory of personal care science. In this context, bakuchiol is not merely a substitute for retinoids but a compelling case study in how holistic sustainability, efficacy, and tolerability can coexist in next-generation cosmetic development.

iv. Sourcing

As discussed previously, *Psoralea corylifolia* has been considered an endangered plant where it is native, therefore consideration for harvesting methods must be paramount (Nabi & Shrivastava, 2017). There is an abundance of literature that supports the use of bakuchiol, from medical and governmental bodies (*India,* 1972; *Government of India, Ministry of AYUSH*, 2001). While it’s status can be considered endangered, this review has shown that it is not just *Psoralea corylifolia* that contain the active bakuchiol, but many other species of *Psoralea* (Mehra *et al.,* 2024; Nabi & Shrivastava, 2017). Additionally, many suppliers of bakuchiol ensure their harvesting

processes are following the Indian Biodiversity Act of 2002. While not a surefire way to ensure sustainable harvest, it provides a starting point for further sustainable practices (*Government of India*, 2002; *Government of India*, 2023). Specific harvesting practices or current labour practices of bakuchiol sourcing are unknown to the public, and often proprietary for each supplier, but are important factors to consider when sourcing *Psoralea corylifolia* and the other related species. Ida *et al.* (2024) studied the impact of local sustainability efforts and how they affect CSR practices, finding that, in Japan, local practices did impact CSR practices at a prefectural, or district, level. While this study didn't show that the local practices extended to corporations, it provides evidence that these practices are important to governments and can even dictate legislation of certain districts. It is not unreasonable to consider that these practices, considering the current state of consumer purchasing behaviour, could eventually extend to the corporate or governmental level. All of this shows that while considered endangered by some bodies, there may be ways to mitigate both ecological and labour practice concerns to bring bakuchiol to mass markets in a holistically sustainable way.

iv. Conclusions

The standards by which ageing is understood and addressed have evolved from valuing wisdom and experience to prioritising aesthetic optimisation and the mitigation of physiological decline. In this transition, the anti-ageing market, now a multi-billion-dollar global industry, has been dominated by active ingredients, particularly retinoids, that function with pharmaceutical intensity. While their clinical efficacy is well established, retinoids continue to pose unresolved challenges, including inflammation, irritation, dryness, and increased photosensitivity. The enduring need to manage or circumvent these adverse effects, despite decades of research, signals an urgent requirement for alternative solutions.

Concurrently, a more informed and ethically conscious consumer base has emerged in the wake of the COVID-19 pandemic. This has intensified the demand for skincare products that are not only effective but aligned with the principles of holistic sustainability, encompassing ecological responsibility, social justice, economic fairness, and regulatory transparency. Within such a vast and commercially aggressive market, this shift in consumer priorities underscores the inadequacy of current ingredient standards and demands innovation that integrates both clinical performance and systemic responsibility.

Bakuchiol offers a compelling and necessary advancement. It mirrors the dermatological efficacy of retinoids across critical pathways, like enhancing collagen production, modulating

pigmentation, regulating sebum, and reducing inflammatory responses, while avoiding their most problematic side effects. Moreover, it offers greater photostability, lower irritation potential, and antibacterial and antifungal properties not shared by retinoids. Importantly, bakuchiol aligns with the growing call for plant-derived, ethically sourced, and environmentally sustainable alternatives. Its extraction from *Psoralea* species, when done in compliance with biodiversity legislation, demonstrates the possibility of harmonising botanical innovation with sustainable harvesting and responsible sourcing.

Given the scale of the anti-ageing market and the limited diversity of well-tolerated, high-efficacy actives, bakuchiol represents not only a scientifically robust alternative but the most viable pathway forward. It addresses the unresolved pharmacological limitations of retinoids, aligns with evolving consumer ethics, and offers a blueprint for integrating holistic sustainability into mainstream cosmetic science and businesses. As this review has demonstrated, bakuchiol is more than a natural mimic, it is a next-generation active that can redefine the future of anti-ageing skincare.

v. References

1. Adarsh Krishna, T.P., Edachery, B. and Athalathil, S. (2022) ‘Bakuchiol – a natural meroterpenoid: Structure, isolation, synthesis and functionalization approaches’, RSC Advances, 12(14), pp. 8815–8832. doi:10.1039/d1ra08771a.

2. Adhikari, S., Joshi, R., Patro, B. S., Ghanty, T. K., Chintalwar, G. J., Sharma, A., Chattopadhyay, S., & Mukherjee, T. (2003) ‘Antioxidant activity of Bakuchiol:

experimental evidences and theoretical treatments on the possible Involvement of the terpenoid chain', Chemical Research in Toxicology, 16(9), pp. 1062–1069. doi:10.1021/tx034082r.

3. Ale, S. I., Laugier, J. P., and Maibach, H. I. (1997). Differential irritant skin responses totandem application of topical RA and sodium lauryl sulphate: II. Effect of time between first and second exposure. The British journal of dermatology, 37(2), 226–233. doi:10.1046/j.1365-2133.1997.18101910.x

4.Altobelli, G.G., Noorden, S. V., Balato, A., Cimini, V. (2020) Scheme of ROS signaling/effects and defense system in the skin. Exogenous and endogenous agents of skin cells generate ROS, whose excessive levels can cause cell damage. ROS modulate MAP signaling pathways leading to activation of the transcription factor AP-1 (activator protein 1) and NF-kB (nuclear factor kappa-light-chain-enhancer of activated B cells). They also induce: (A) a decrease in procollagen synthesis via blocking TGF-β/SMAD signaling; (B) an increase in the inflammatory processes; (C) an increase in collagen degradation via synthesis of matrix degenerating MMPs. Furthermore, ROS allow nuclear factor Nrf2 to detach from its cytoplasmic inhibitor, keap-1, to translocate to the nucleus and activate transcription of antioxidant genes. Melatonin (8) and α-MSH (9) are also stimulated by ROS to activate Nrf2 dependent-pathways and then the expression of antioxidant genes. The Nrf2 pathway is activated not only in different skin cells such as keratinocytes and melanocytes, but also in fibroblasts (10). Modified by Sardy (11)., Copper/Zinc Superoxide Dismutase in Human Skin: Current Knowledge. Frontiers in Medicine. Available at: 10.3389/fmed.2020.00183 (Accessed: August 2025).

5. Amici, J.M., Cogrel, O., Jourdan, M., Raimbault, C., Canchy, L., Kerob, D., Madfes, D.C., Tian, Y., Araviiskaia, E. Amici, J. (2023) 'Expert recommendations on supportive skin care for non-surgical and surgical procedures', Journal of the European Academy of Dermatology and Venereology, 37(S3), pp. 16–33. doi:10.1111/jdv.18855.

6. Amirrah, I. N., Lokanathan, Y., Zulkiflee, I., Wee, M. F. M. R., Motta, A., & Fauzi, M. B. (2022). A Comprehensive Review on Collagen Type I Development of Biomaterials for Tissue Engineering: From Biosynthesis

to Bioscaffold. Biomedicines, 10(9), 2307. https://doi.org/10.3390/biomedicines10092307

7. Asl, E.R., Amini, M., Najafi, S., Mansoori, B., Mokhtarzadeh, A., Mohammadi, A., Lotfinejad, P., Bagheri, M., Shirjang, S., Lotfi, Z., Rasmi, Y., Baradaran, B. (2021) 'Interplay between MAPK/ERK signaling pathway and micrornas: A crucial mechanism regulating cancer cell metabolism and tumor progression', Life Sciences, 278, p. 119499. doi:10.1016/j.lfs.2021.119499.

8. Babina, M., Guhl, S., Motakis, E., Artuc, M., Hazzan, T., Worm, M., Forrest, A., Zuberbier, T. (2015) 'RA potentiates inflammatory cytokines in human mast cells: Identification of mast cells as prominent constituents of the skin retinoid network', Molecular and Cellular Endocrinology, 406, pp. 49–59. doi:10.1016/j.mce.2015.02.019.

9. Bacqueville, D., Maret, A., Noizet, M., Duprat L, Coutanceau, C., Georgescu, V.,Bessou-Touya, S., Duplan, H. (2020) 'Efficacy of a dermocosmetic serum combining bakuchiol and vanilla tahitensis extract to prevent skin photoageing *in vitro* and to improve clinical outcomes for naturally aged skin</p>', Clinical, Cosmetic and Investigational Dermatology, Volume 13, pp. 359–370. doi:10.2147/ccid.s235880.

10. Baker, P. Huang, C., Radi, R., Moll, S.B., Jules, E., Arbiser, J.L. (2023) 'Skin barrier function: The interplay of physical, chemical, and immunologic properties', Cells, 12(23), p. 2745.doi:10.3390/cells12232745.

11. Barbieri, J.S., Wanat, K. and Seykora, J. (2014) 'Skin: Basic structure and function', Pathobiology of Human Disease, pp. 1134–1144. doi:10.1016/b978-0-12-386456-7.03501-2.

12. Beckenbach, L. Baron, J., Merk, H., Loffler, H., Amann, P. (2015) 'Retinoid treatment of skin diseases,' European journal of dermatology : EJD, 25(5), 384–391. https://doi.org/10.1684/ejd.2015.2544

13. Berger, T.G. and Steinhoff, M. (2011) 'Pruritus in elderly patients—eruptions of

senescence', Seminars in Cutaneous Medicine and Surgery, 30(2), pp. 113–117. doi:10.1016/j.sder.2011.04.002.

14. Blasco, M.A. (2007) 'Telomere length, stem cells and ageing', Nature Chemical Biology, 3(10), pp. 640–649. doi:10.1038/nchembio.2007.38.

15. Bluemke, A., Ring, A.P., Immeyer, J., Hoff, A., Eisenberg, T., Gerwat, W., Meyer, F., Breitkreutz, S., Klinger, L.M., Brandner, J.M., Sandig, G., Seifert, M., Segger, D., Rippke, F., Schweiger, D. et al. (2022) 'Multidirectional activity of Bakuchiol against cellular mechanisms of facial ageing - experimental evidence for a holistic treatment approach', International Journal of Cosmetic Science, 44(3), pp. 377–393. doi:10.1111/ics.12784.

16. Bolognia, J.L., Braverman, I.M., Rousseau, M.E., Sarrel P.M. (1989) 'Skin changes in Menopause', Maturitas, 11(4), pp. 295–304. doi:10.1016/0378-5122(89)90026-1.

17. Bolognia, J.L., Schaffer, J.V., Cerroni, L. et al. (2012). "Ageing Skin," American Journal of Clinical Dermatology13, pp. 435–448.

18. Bom, S., Ribeiro, H.M. and Marto, J. (2020) 'Sustainability calculator: A tool to assess sustainability in cosmetic products', *Sustainability*, 12(4), p. 1437. doi:10.3390/su12041437.

19. Bornstein, P. (1974) 'The biosynthesis of collagen', Annual Review of Biochemistry, 43(1), pp. 567–603. doi:10.1146/annurev.bi.43.070174.003031.

20. Bouwstra, J.A. Gooris, G.S., Bras, W., Downing, D.T. (1995) 'Lipid organization in pig SC.', Journal of Lipid Research, 36(4), pp. 685–695. doi:10.1016/s0022-2275(20)40054-9.

21. Brincat, M., Moniz, C.F., Studd, J.W., Darby, A.J., Magos, A., Cooper, D. (1983) 'Sex hormones and skin collagen content in postmenopausal women.',

BMJ, 287(6402), pp. 1337–1338. doi:10.1136/bmj.287.6402.1337.

22. Brown, Furmanczyk, M., Ramos, D., Ribes, A., Pons, L., Bustois, J., de Henestrosa, A. Granger, C., Jourdan, E. (2023). 'Natural retinol analogs potentiate the effects of retinol on aged and photodamaged skin: Results from *in vitro* to clinical studies', Dermatology and Therapy, 13(10), pp. 2299-2317. doi:10.1007/s13555-023-01004-z.

23. Bulengo-Ransby, S.M., Griffiths, C.E., Kimbrough-Green, C.K., Finkel, L., Hamilton, T.A., Ellis, C.N., Voorhees, J.J. (1993) 'Topical tretinoin (RA) therapy for hyperpigmented lesions caused by inflammation of the skin in black patients', New England Journal of Medicine, 328(20), pp. 1438–1443. doi:10.1056/nejm199305203282002.

24. Cadet, J., Douki, T. and Ravanat, J. (2014) 'Oxidatively generated damage to cellular dna by uvb and uva radiation,' Photochemistry and Photobiology, 91(1), pp. 140–155. doi:10.1111/php.12368.

25. Campisi, J. and d'Adda di Fagagna, F. (2007) 'Cellular senescence: When bad things happen to good cells', Nature Reviews Molecular Cell Biology, 8(9), pp. 729–740. doi:10.1038/nrm2233.

26. Campuzano-García, A.E., Torres-Alvarez, B., Hernandrez-Blar, D., Funetes-Ahuma, C., Cortes-Garcia, J.D., Castanedo-Cazares, J. et al. (2019) 'DNA methyltransferases in Malar Melasma and their modification by Sunscreen in combination with 4% niacinamide, 0.05% RA, or placebo', BioMed Research International, 2019, pp. 1–7. doi:10.1155/2019/9068314.

27. Cenizo, V., André, V., Reymermier, C., Sommer, P., Damour, O., Perrier, E. (2006) 'LOXL as a target to increase the elastin content in adult skin: A dill extract induces the LOXL gene expression', Experimental Dermatology, 15(8), pp. 574–581. doi:10.1111/j.1600-0625.2006.00442.x.

28. Cestari, T.F., Dantas, L.P. and Boza, J.C. (2014) 'Acquired Hyperpigmentations', Anais Brasileiros de Dermatologia, 89(1), pp. 11– doi:10.1590/abd1806-4841.20142353.

29. Chaudhuri, R. K., and Bojanowski, K. (2014) ‘Bakuchiol: a retinol-like functional compound revealed by gene expression profiling and clinically proven to have anti-ageing effects,’ International journal of cosmetic science, 36(3), 221–230. doi:/10.1111/ics.12117

30. Chen, L., Hu, Y., Wang, W. (2012) “Chronic Inflammation and Skin Ageing,” Journal of Dermatology, 39, pp.751–759.

31. Chen, W., Li, J., Ma, Y., Shi, R., Yu, H., Gantumur, M.-A., Bilawal, A., Jiang, Z. (2023) ‘Binding interaction and stability of alpha-lactalbumin and retinol: Effects of pre- or post-acidification’, Food Hydrocolloids, 135, p. 108140. doi:10.1016/j.foodhyd.2022.108140.

32. Chen, S., Ostrowski, J., Whiting, G., Roalsvig, T., Hammer, L., Currier, S.J., Honeyman, J., Kwasniewski, B., Yu, K.L., Sterzycki, R. (1995). Retinoic acid receptor gamma mediates topical retinoid efficacy and irritation in animal models. The Journal of investigative dermatology, 104(5), 779 –783. https://doi.org/10.1111/1523-1747.ep12606988

33. Chen, S.J., Yuan, W., Lo, S., Trojanowska, M., Varga, J. et al. (2000) ‘Interaction of smad3 with a proximal SMAD-binding element of the human α2(i) procollagen gene promoter required for transcriptional activation by TGF-β’, Journal of Cellular Physiology, 183(3), p. 381. doi:10.1002/(sici)1097-4652(200006)183:3<381::aid-jcp11>3.3.co;2 -f.

34. Chen, S.J., Yuan, W., Mori, Y., Levenson, A., Trojanowska, M., Varga, J. et al. (1999) ‘Stimulation of type I collagen transcription in human skin fibroblasts by TGF-β: Involvement of Smad 3’, Journal of Investigative Dermatology, 112(1), pp. 49–57. doi:10.1046/j.1523-1747.1999.00477.x.

35. Chen, Z., Seo, J.Y., Kim, Y.K., Lee, S.R., Kim, K.H., Cho, K.H., Eun, H.C., Chung, J.H. (2005) ‘Heat modulation of tropoelastin, fibrillin-1, and matrix metalloproteinase-12 in human skin in vivo’, Journal of Investigative

Dermatology, 124(1), pp. 70–78. doi:10.1111/j.0022-202x.2004.23550.x.

36. Chen, Z., Shin, M.H., Moon, Y.J., Lee, S.R., Kim, Y.K., Seo, J.E., Kim, J.E., Kim, K.H., Chung, J.H. et al. (2009) 'Modulation of elastin exon 26a mrna and protein expression in human skin in vivo', Experimental Dermatology, 18(4), pp. 378–386. doi:10.1111/j.1600 -0625.2008.00799.x.

37. Chien, A.L., Qi, J., Grandhi, R., Kim, N., Cesar, S.S., Harris-Tryon, T., Jang, M.S., Olowoyeye, O., Kuhn, D., Leung, S., Rainer, B.M.Poon, F., Suh, J., Cheng, N., Okoye, G.A., Kang, S. (2018) 'Effect of age, gender, and sun exposure on ethnic skin photoageing: Evidence gathered using a new photonumeric scale', Journal of the National Medical Association, 110(2), pp. 176–181. doi:10.1016/j.jnma.2017.05.001.

38. Choi, S.Y., Bin, B.H., Kim, W., Lee, E., Lee, T.R., Cho, E.G. (2018) 'Exposure of human melanocytes to UVB twice and subsequent incubation leads to cellular senescence and senescence-associated pigmentation through the prolonged p53 expression', Journal of Dermatological Science, 90(3), pp. 303–312. doi:10.1016/j.jdermsci.2018.02.016.

39. Chung, K.Y., Agarwal, A., Uitto, J., Mauviel, A. et al. (1996) 'An AP-1 binding sequence is essential for regulation of the human α2(i) collagen (COL1A2) promoter activity by transforming growth factor-β', Journal of Biological Chemistry, 271(6), pp. 3272–3278. doi:10.1074/jbc.271.6.3272.

40. Chung, J.H., Seo, J.Y., Lee, M.K., Eun, H.C., Lee, J.H., Kang, S., Fisher, G., Voorhees, J.J. Chung, J.H. et al. (2002) 'Ultraviolet modulation of human macrophage Metalloelastase in human skin in vivo', Journal of Investigative Dermatology, 119(2), pp. 507–512. doi:10.1046/j.1523 -1747.2002.01844.x.

41. Cole, M.A.; Quan, T.; Voorhees, J.J.; Fisher, G.J. et al. (2018) 'Extracellular matrix regulation of fibroblast function: Redefining our perspective on

Skin ageing', Journal of Cell Communication and Signaling, 12(1), pp. 35 –43. doi:10.1007/s12079-018-0459-1.

42. Colombo, F., Alfano, S. and Milani, M. (2025) 'Lipidomic and instrumental evaluation of a melatonin-based in & out strategy versus topical treatment in skin ageing: A randomized prospective trial', Metabolites, 15(1), p. 33. doi:10.3390/metabo15010033.

43. Commission regulation (EU) 2024/996 amending regulation (EC) no 1223/2009 of the European Parliament and of the Council. (2022) Home. Available at: https://www.creme.uk.com/blog/ec-regulation-2024-996 ISSN 1977-0677 (electronic edition)

44. Crocco, E. I., Bonifácio, E. B., Facchini, G., da Silva, G. H., da Silva, M. S., Pinheiro, A. L. T. A., Avelar, P. V. F., Eberlin, S. (2021). Modulation of skin androgenesis and sebum production by a dermocosmetic formulation. Journal of cosmetic dermatology, 20(1), 360 –365.doi:10.1111/jocd.13503.

45. D'Arcangelis A., Goswami Chatterjee S., Diaz I., Guehenneux S., Namkoong J., Wu J. (2024) '*In vitro*, *ex vivo*, instrumental and clinical evaluation of a topical cream on the signs of periorbital ageing', International Journal of Cosmetic Science, 47(1), pp. 18–30. doi:10.1111/ics.12987.

46. David, M., Hodak, E. and Lowe, N.J. (1988) 'Adverse effects of retinoids', Medical Toxicology, 3(4), pp. 273–288. doi:10.1007/bf03259940.

47. Davis, A., Furtak, A., Paterson, S., Velthuizen, R., Shen, J., Nip, J., Bappal, A., Lathrop, W., Villa, A., Lee, J-M., Guelakis, M. (2024) 'Topical application of retinyl propionate, 4 hexyl resorcinol, and Niacinamide Reverses Molecular and clinical features of Ageing', International Journal of Cosmetic Science, 46(5), pp. 761–774. doi:10.1111/ics.12958.

48. Delannoy, A., Baudier, P. and de Vassoigne, T. (2023) 'Perceptions of ethical

cosmetics: Health behaviors during the covid-19 pandemic', Journal of Consumer Behaviour, 23(2), pp. 470–490. doi:10.1002/cb.2215.

49. Dlamini, S. and Mahowa, V. (2024) 'Investigating factors that influence the purchase behaviour of Green Cosmetic Products', Cleaner and Responsible Consumption, 13, p. 100190. doi:10.1016/j.clrc.2024.100190.

50. Dubey, R., Shami, T.C. and Bhasker-Rao, K.U. (2009). Microencapsulation Technology and Applications. Defence Science Journal. 59. 82. 10.14429/dsj.59.1489.

51. ECHA: European chemicals agency (2022) Registration dossier - ECHA. Available at: https://echa.europa.eu/registration-dossier/-/registered-dossier/17106/2/1 -ECHA: European chemicals agency (2022p) Registration dossier: bakuchiol. https://echa.europa.eu/pt/registrationdossier/-/registered-dossier/17106/5/3/2. [Accessed 05 Jul 2022].

52. Failloux, N., Bonnet, I., Perrier, E., Baron, M.H. et al. (2004) 'Effects of light, oxygen and concentration on vitamin A1', Journal of Raman Spectroscopy, 35(2), pp. 140–147. doi:10.1002/jrs.1116.

53. Farage, M.A., Miller, K.W., Elsner, P. and Maibach, H.I. (2008) 'Intrinsic and extrinsic factors in skin ageing: A Review', International Journal of Cosmetic Science, 30(2), pp. 87–95. doi:10.1111/j.1468-2494.2007.00415.x.

54. Farris, P.K. and Rendon, M.I. (2010) 'The mechanism of action of the topical retinoids for the treatment of nonmalignant photodamage', Cosmetic Dermatology, 23(1), pp.108–9.

55. Farris P. (2022) SUPPLEMENT ARTICLE: Retinol: The Ideal Retinoid for Cosmetic Solutions. Journal of drugs in dermatology : JDD, 21(7), s4 –s10. doi:10.36849/JDD.SO722

56. Fayad, S., Morin, P. and Nehmé, R. (2017) 'Use of chromatographic and electrophoretic tools for assaying elastase, collagenase, hyaluronidase, and tyrosinase activity', Journal of Chromatography A, 1529, pp. 1–28. doi:10.1016/j.chroma.2017.11.003.

57. Ferrandiz, M.L., Gil, B., Sanz, M.J., Ubeda, A.m Erazo, S., Gonzalez, E., Negrete, R., Pacheco, S., Payaa, M., Alcaraz, M. et al. (1996) 'Effect of bakuchiol on leukocyte functions and some inflammatory responses in mice', Journal of Pharmacy and Pharmacology, 48(9), pp. 975–980. doi:10.1111/j.2042-7158.1996.tb06016.x.

58. Finkel, T. and Holbrook, N.J. (2000) 'Oxidants, oxidative stress and the biology of ageing', Nature, 408(6809), pp. 239–247. doi:10.1038/35041687.

59. Fisher, G.J., Datta, S.C., Talwar, H.S., Wang, Z.-Q., Varani, J., Kang, S., Voorhees, J.J. (1996) 'Molecular basis of sun-induced premature skin ageing and retinoid antagonism', Nature, 379(6563), pp. 335–339. doi:10.1038/379335a0.

60. Fisher, G.J., Quan, T., Purohit, T., Shao, Y., Cho, M., He, T., Varani, J., Kang, S., Voorhees, J.J. (2009) 'Collagen fragmentation promotes oxidative stress and elevates matrix metalloproteinase-1 in fibroblasts in aged human skin', The American Journal of Pathology, 174(1), pp. 101–114. doi:10.2353/ajpath.2009.080599.

61. Fisher, G.J., Varani, J. and Voorhees, J.J. (2008) 'Looking older: Fibroblast collapse and therapeutic implications', Archives of Dermatology, 144(5), pp. 666-672. doi:10.1001/archderm.144.5.666.

62. Fisher, G.J., Kang, S., Varani, J., Bata-Csirgo, Z., Wan, Y., Datta, S., Voorhees, J.J. (2002) 'Mechanisms of photoageing and chronological skin ageing', Archives of Dermatology, 138(11). doi:10.1001/archderm.138.11.1462 -70.

63. Fisher G.J., Wang Z.Q., Datta S.C., Varani J., Kang S, Voorhees JJ. (1997) 'Pathophysiology of premature skin ageing induced by ultraviolet light',

New England Journal of Medicine, 337(20), pp. 1419–1429. doi:10.1056/nejm199711133372003.

64. Fisher, G.J.; Shao, Y.; He, T.; Qin, Z.; Perry, D.; Voorhees, J.J.; Quan, T. (2015) 'Reduction of fibroblast size/mechanical force down-regulates tgf -β type ii receptor: Implications for human skin ageing', Ageing Cell, 15(1), pp. 67–76. doi:10.1111/acel.12410.

65. Fisher, G.J. and Voorhees, J.J. (1998) 'Molecular mechanisms of photoageing and its prevention by RA: Ultraviolet irradiation induces MAP kinase signal transduction cascades that induce AP-1-regulated matrix metalloproteinases that degrade human skin in vivo', Journal of Investigative Dermatology Symposium Proceedings, 3(1), pp. 61–68. doi:10.1038/jidsymp.1998.15.

66. Fitsiou, E., Pulido, T., Campisi, J., Alimirah, F., Demaria, M. Ce Fitsiou, E. (2021) 'Cellular senescence and the senescence-associated secretory phenotype as drivers of skin photoageing', Journal of Investigative Dermatology, 141(4), pp. 1119–1126. doi:10.1016/j.jid.2020.09.031.

67. Flament, F. Bazin, R., Laquieze, S. Rubert, V., Simonpietri, E. and Piot, B. (2013) 'Effect of the sun on visible clinical signs of ageing in Caucasian skin', Clinical, Cosmetic and Investigational Dermatology, pp. 221–232. doi:10.2147/ccid.s44686.

68. Fluhr, J.W., Vienne, M.P., Lauze, C., Dupuy, P., Gehring, W., Gloor, M. et al. (1999) 'Tolerance profile of retinol, retinaldehyde and RA under maximized and long-term clinical conditions', Dermatology, 199(Suppl. 1), pp. 57–60. doi:10.1159/000051381.

69. Ganceviciene, R., Liakou, A.I., Theodoridis, A., Makrantonaki, E., and Zouboulis, C.C. (2012) 'Skin anti-ageing strategies', Dermato-Endocrinology, 4(3), pp. 308–319. doi:10.4161/derm.22804.

70. Gelain, D.P. Pasquali, M., Caregnato, F., Moreira, J.C. et al. (2011) 'Vitamin A

(retinol) up-regulates the receptor for advanced glycation endproducts (RAGE) through p38 and Akt oxidant-dependent activation', Toxicology, 289(1), pp. 38–44. doi:10.1016/j.tox.2011.07.008.

71. Gericke J., Ittensohn J., Miha´ly J., Alvarez, S., Torocsik D., de Lera A.R., Ruhl, R. (2013) 'Regulation of retinoid-mediated signaling involved in skin homeostasis by RAR and RXR agonists/antagonists in mouse skin', PLoS ONE, 8(4). doi:10.1371/journal.pone.0062643.

72. Ghosh, A.K., Yuan, W., Mori, Y., Varga, J. (2000) 'Smad-dependent stimulation of type I collagen gene expression in human skin fibroblasts by TGF-β involves functional cooperation with P300/CBP transcriptional coactivators', Oncogene, 19(31), pp. 3546–3555. doi:10.1038/sj.onc.1203693.

73. Godeau, G. and Hornebeck, W. Morphometric analysis of the degradation of human skin elastic fibres by human leukocyte elastase (EC 3-4-21-37) and human skin fibroblast elastase (EC 3-4-24). Pathol Biol (Paris). 1988 Nov;36(9):1133-8. PMID: 3065704.

74. Goldberg, E.L. and Dixit, V.D. (2015) 'Drivers of age-related inflammation and strategies for healthspan extension', Immunological Reviews, 265(1), pp. 63–74. doi:10.1111/imr.12295.

75. Government of India, 2002. The Biological Diversity Act, 2002. New Delhi: Ministry of Law and Justice. [Last updated 5 February 2003]. New Delhi: Government of India. Available at: https://www.indiacode.nic.in/bitstream/123456789/2046/4/a2003-18.pdf (Accessed: 20/5/25).

76. Government of India, 2023. The Biological Diversity (Amendment) Act, 2023. New Delhi: Ministry of Law and Justice. [Last updated 3 August 2023]. New Delhi: Government of India. Available at: https://egazette.gov.in/WriteReadData/2023/247815.pdf (Accessed: 20/5/25).

77. Government of India, Ministry of AYUSH, 2001. The Ayurvedic Pharmacopoeia of India: Part I, Volume I. New Delhi: Government of India Press. [Last updated 1978]. New Delhi: Government of India. Available at: https://www.ayurveda.hu/api/API-Vol-1.pdf (Accessed: 20/5/25).

78. Gray, W.R., Sandberg, L.B. and Foster, J.A. (1973) 'Molecular model for elastin structure and function', Nature, 246(5434), pp. 461–466. doi:10.1038/246461a0.

79. Griffiths, C.E. (2001) 'The role of retinoids in the prevention and repair of aged and photoaged skin', Clinical and Experimental Dermatology, 26(7), pp. 613–618. doi:10.1046/j.1365-2230.2001.00892.x.

80. Grimes, P.E. (1995) 'Melasma: Etiologic and Therapeutic Considerations. Arch Dermatol., 131(12), pp.1453–1457. doi:10.1001/archderm.1995.01690240119022

81. Gu, Y., Bell, G., Rasheed, A., Beldona, S. (2024). 'Commitment to values: Examining the role of ethical and responsible business practices on short and long-term value', Business and Society Review, 129(1), pp. 96-129. Doi:10.1111/basr.12344.

82. Halai, P., Kiss, O., Wang, R., Chien, A., Kang, S., O'Conner, C., Bell, M., Griffiths, C.E., Watson, R.E., Langton, A.K. (2024) 'Retinoids in the treatment of photoageing: A histological study of topical retinoid efficacy in black skin', Journal of the European Academy of Dermatology and Venereology, 38(8), pp. 1618–1627. doi:10.1111/jdv.20043.

83. Han, J., Gong, R., Liu, Y., Gong, T., Wang, B. Zhang, L. Chen, J. (2025) 'A novel microcapsule composite spherulites peony superior retinol mitigate uvb-induced skin damage *in vitro* and in vivo', Photochemistry and Photobiology [Preprint]. doi:10.1111/php.14078.

84. Harrison, E.H. (2012) 'Mechanisms involved in the intestinal absorption of dietary vitamin A and provitamin A carotenoids', Biochimica et Biophysica Acta (BBA) - Molecular and Cell Biology of Lipids, 1821(1), pp. 70–77. doi:10.1016/j.bbalip.2011.06.002.

85. Heilman, M.E. and Stopeck, M.H. (1985) ‘Being attractive, advantage or disadvantage? performance-based evaluations and recommended personnel actions as a function of appearance, sex, and job type’, Organizational Behavior and Human Decision Processes, 35(2), pp. 202 –215. doi:10.1016/0749-5978(85)90035-4.

86. Herndon, J. H., Jr, Jiang, L. I., Kononov, T., and Fox, T. (2016) ‘An Open Label Clinical Trial to Evaluate the Efficacy and Tolerance of a Retinol and Vitamin C Facial Regimen in Women With Mild-to-Moderate Hyperpigmentation and Photodamaged Facial Skin’, Journal of Drugs in Dermatology, 15(4), 476-482. PMID: 27050703.

87. Huckle, J., and Wals, A. E. J. (2015) ‘The UN Decade of Education for Sustainable Development: business as usual in the end,’ Environmental Education Research, 21(3), 491–505. doi:10.1080/13504622.2015.1011084

88. Ida, A. Yoshida, K., Xie, J., Tanaka, Y. Managi, S. (2024) ‘Do local government sustainability initiatives impact corporate social sustainability practices?’, Business Strategy and the Environment, 33(6), pp. 5839–5854. doi:10.1002/bse.3780.

89. Ignotz, R.A. and Massagué, J. (1986) ‘Transforming growth factor-beta stimulates the expression of fibronectin and collagen and their incorporation into the extracellular matrix.’, Journal of Biological Chemistry, 261(9), pp. 4337–4345. doi:10.1016/s0021-9258(17)35666-1.

90. Ilkit, M. and Durdu, M. (2014) ‘Tinea pedis: The etiology and global epidemiology of a common fungal infection’, Critical Reviews in Microbiology, 41(3), pp. 374–388. doi:10.3109/1040841x.2013.856853.].

91. Irby, C.E., Yentzer, B.A. and Feldman, S.R. (2008) ‘A review of adapalene in the treatment of Acne Vulgaris’, Journal of Adolescent Health, 43(5), pp. 421–424. doi:10.1016/j.jadohealth.2008.06.005.

92. IUPAC-IUB Joint Commission on Biochemical Nomenclature (JCBN), "Nomenclature of Retinoids," European Journal of Biochemistry, 129, 1-5, 1982. Accessed: [20/5/25]. Available at: https://pubmed.ncbi.nlm.nih.gov/7160373/

93. Jafernik, K, Halina, E., Ercisli, S., Szopa, A. et al. (2020) 'Characteristics of bakuchiol - the compound with high biological activity and the main source of its acquisition - cullen corylifolium (L.) medik', Natural Product Research, 35(24), pp. 5828–5842. doi:10.1080/14786419.2020.1837813.

94. Ji, M. and Yu, Q. (2015) 'Primary osteoporosis in postmenopausal women', Maturitas, 82(3), p. 315. doi:10.1016/j.maturitas.2015.06.009.

95. Jourdan, M., Madfes, D.C., Lima, E., Tian, Y., Seité, S. et al. (2019) 'Skin care management for medical and aesthetic procedures to prevent scarring', Clinical, Cosmetic and Investigational Dermatology, Volume 12, pp. 799–804. doi:10.2147/ccid.s218134.

96. Kamm, J.J. (1982) 'Toxicology, carcinogenicity, and teratogenicity of some orally administered retinoids', Journal of the American Academy of Dermatology, 6(4), pp. 652–659. doi:10.1016/s0190-9622(82)70054-4.

97. Kang, S., Fisher, G.J. and Voorhees, J.J. (2001) 'Photoageing', Clinics in Geriatric Medicine, 17(4), pp. 643–659. doi:10.1016/s0749 -0690(05)70091-4.

98. Kang, M.C., Lee, J.W., Lee, T., Subedi, L., Wahedi, H.M., Do, S.G., Shin, E., Moon, E.Y., Kim, S.Y. et al. (2020) 'UP256 inhibits hyperpigmentation by tyrosinase expression/dendrite formation via rho-dependent signaling and by primary cilium formation in melanocytes', International Journal of Molecular Sciences, 21(15), p. 5341. doi:10.3390/ijms21155341.

99. Kapoor, R., Singh, A.B. and Misra, R. (2019) 'Green cosmetics – changing young consumer preference and reforming cosmetic industry', International Journal of Recent Technology and Engineering, 8(4), pp.

12932–12939. doi:10.35940/ijrte.d6927.118419.

100. Kawanishi, S. and Oikawa, S. (2004) ‘Mechanism of telomere shortening by oxidative stress’, Annals of the New York Academy of Sciences, 1019(1), pp. 278–284. doi:10.1196/annals.1297.047.

101. Kaya, G. and Saurat, J.-H. (2007) ‘Dermatoporosis: A chronic cutaneous insufficiency/fragility syndrome’, Dermatology, 215(4), pp. 284–294. doi:10.1159/000107621.

102. Khalil, S., Bardawil, T., Stephan, C., Darwiche, N., Abbas, O., Kibbi, A.G., Nemer, G., Kurban, M. (2017) ‘Retinoids: A journey from the molecular structures and mechanisms of action to clinical uses in dermatology and adverse effects’, Journal of Dermatological Treatment, 28(8), pp. 684 –696. doi:10.1080/09546634.2017.1309349.

103. Khosla, S. (2012) ‘Pathogenesis of age-related bone loss in humans’, The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 68(10), pp. 1226–1235. doi:10.1093/gerona/gls163.

104. Kim, D.J., Iwasaki, A., Chien, A.L., Kang, S. (2022) Proposed model for MMP induction in photoageing., UVB-mediated DNA damage induces matrix metalloproteinases to promote photoageing in an AhR- and SP1-dependent manner. Journal of Clinical Investigation. Available at: https://doi.org/10.1172/jci.insight.156344 (Accessed: July 2025).

105. Kielty, C.M., Sherratt, M.J. and Shuttleworth, C.A. (2002) ‘Elastic fibres’, Journal of Cell Science, 115(14), pp. 2817–2828. doi:10.1242/jcs.115.14.2817.

106. Kim, H., Kim, B., Kim, H., Um, S., Lee, J., Ryoo, H., Jung, H. et al. (2008) ‘Synthesis and *in vitro* biological activity of retinyl retinoate, a novel hybrid retinoid derivative’, Bioorganic & Medicinal Chemistry, 16(12), pp. 6387–6393. doi:10.1016/j.bmc.2008.05.005.

107. Kim JE, Kim JH, Lee Y, Yang, H., Heo, Y.S., Bode, A., Lee, K., Dong, Z. Kim, J.-E. et al. (2016) ‘Bakuchiol suppresses proliferation of skin cancer cells

by directly targeting Hck, BLK, and P38 Map Kinase', Oncotarget, 7(12), pp. 14616–14627. doi:10.18632/oncotarget.7524.

108. Knight, J., Andrade , M. and Bayram-Weston, Z. (2024) Vitamin A and related molecules, Vitamins A and C: their function and structure explained. EMAP Publishing Limited. Available at: https://www.nursingtimes.net/nutrition-and-hydration/vitamins-a-and-c-their-function-and-structure-explained-29-01-2024/ (Accessed: July 2025).

109. Kong, R., Cui, Y., Fisher, G.J., Wang, X., Chen, Y., Schneider, L.M., Majmudar, G. (2015) 'A comparative study of the effects of retinol and RA on histological, molecular, and clinical properties of human skin', Journal of Cosmetic Dermatology, 15(1), pp. 49–57. doi:10.1111/jocd.12193.

110. Langton, A.K., Alessi, S., Hann, M., Chien, A.L., Kang, S., Griffiths, C.E., Watson, R.E. et al. (2019) 'Ageing in skin of color: Disruption to elastic fiber organization is detrimental to skin's biomechanical function', Journal of Investigative Dermatology, 139(4), pp. 779–788. doi:10.1016/j.jid.2018.10.026.

111. Lau, K.-M. Wong, J.H., Wu, W.-O., Cheng, L., Wong, C.-W., To, M.-H., Lau, C.P., Yew, D.T., Leung, P.-C., Fung, K.-P., Hui, M., Ng, T.B., Lauet, C. (2014) 'Anti-dermatophytic activity of Bakuchiol: *In vitro* mechanistic studies and in vivo tinea pedis-inhibiting activity in a guinea pig model', Phytomedicine, 21(7), pp. 942–945. doi:10.1016/j.phymed.2014.03.005.

112. Lee, E.-S.; Ahn, Y.; Bae, I.-H.; Min, D.; Park, N.H.; Jung, W.; Kim, S.-H.; Hong, Y.D.; Park, W.S.; Lee, C.S. et al. (2020) 'Synthetic retinoid seletinoid g improves skin barrier function through wound healing and collagen realignment in human skin equivalents', International Journal of Molecular Sciences, 21(9), p. 3198. doi:10.3390/ijms21093198

113. Lee, J. and Kwon, K.H. (2022) 'Sustainable changes in beauty market trends focused on the perspective of safety in the post-coronavirus disease-19 period', Journal of Cosmetic Dermatology, 21(7), pp. 2700–2707.

doi:10.1111/jocd.14493.

114. Lee, D.-D., Stojadinovic, O., Krzyzanowska, A., Vouthounis, C., Blumenberg, M., Tomic-Canic, M. (2009) 'Retinoid-responsive transcriptional changes in epidermal keratinocytes', Journal of Cellular Physiology, 220(2), pp. 427–439. doi:10.1002/jcp.21784.

115. Lee, S.C., Yuk, H.G., Lee, D.H., Lee, K.E., Hwang, Y.I., Ludescher, R.D. (2002) 'Stabilization of retinol through incorporation into liposomes' , BMB Reports, 35(4), pp. 358–363. doi:10.5483/bmbrep.2002.35.4.358.

116. Lemaitre, J. (2024) 'Looking for the philosopher's stone: Emerging approaches to target the hallmarks of ageing in the skin', Journal of the European Academy of Dermatology and Venereology, 38(S4), pp. 5–14. doi:10.1111/jdv.19820.

117. Lephart, E.D. (2018) 'A review of the role of estrogen in dermal ageing and facial attractiveness in women', Journal of Cosmetic Dermatology, 17(3), pp. 282–288. doi:10.1111/jocd.12508.

118. Lephart, E.D. and Naftolin, F. (2020) 'Menopause and the skin: Old favorites and new innovations in cosmeceuticals for estrogen-deficient skin', Dermatology and Therapy, 11(1), pp. 53–69. doi:10.1007/s13555-020-00468-7.

119. Lewińska, A., Domżał-Kędzia, M., Maciejczyk, E., Łukaszewicz, M., & Bazylińska, U. (2021). Design and Engineering of "Green" Nanoemulsions for Enhanced Topical Delivery of Bakuchiol Achieved in a Sustainable Manner: A Novel Eco-Friendly Approach to Bioretinol. International Journal of Molecular Sciences, 22(18), 10091. doi:10.3390/ijms221810091

120. Li, J., Li, Q. and Geng, S. (2019) 'All-trans RA alters the expression of the tight junction proteins claudin-1 and -4 and epidermal barrier function-associated genes in the epidermis', International Journal of Molecular Medicine [Preprint]. doi:10.3892/ijmm.2019.4098.

121. Li, Z.; Niu, X.; Xiao, S.; Ma, H. et al. (2017) ‘RA ameliorates photoaged skin through RAR-mediated pathway in mice’, Molecular Medicine Reports, 16(5), pp. 6240–6247. doi:10.3892/mmr.2017.7336.

122. Lystvan, K. Belokurova, V., Sheludko, Y., Ingham, J.L., Prykhodko, V., Kishchenko, O., Paton, E., Kuchuk M. et al. (2009) ‘Production of Bakuchiol by *in vitro* systems of PSORALEA DRUPACEA BGE’, Plant Cell, Tissue and Organ Culture (PCTOC), 101(1), pp. 99–103. doi:10.1007/s11240-009-9657-0.

123. Mao, T., Jiang, Z., Han, Y., Teng, W., Zhao, X., Li, W. (2013) ‘Identification of quantitative trait loci underlying seed protein and oil contents of soybean across multi-genetic backgrounds and environments’, Plant Breeding, 132(6), pp. 630–641. doi:10.1111/pbr.12091.

124. Madhumita, M. and Ponnarasu, S. (2024) ‘Nurturing youth: Ethical considerations in pediatric skincare marketing’, Pediatric Dermatology, 42(2), pp. 428–431. doi:10.1111/pde.15796.

125. Matsuda, H, Kiyohara, S., Sugimoto, S., Ando, S., Nakamura, S., Yoshikawa, M. (2009) ‘Bioactive constituents from Chinese natural medicines. XXXIII. inhibitors from the seeds of Psoralea corylifolia on production of nitric oxide in lipopolysaccharide-activated macrophages’, Biological and Pharmaceutical Bulletin, 32(1), pp. 147–149. doi:10.1248/bpb.32.147.

126. Mecham, R.P. (1991) ‘Elastin synthesis and fiber assemblya’, Annals of the New York Academy of Sciences, 624(1), pp. 137–146. doi:10.1111/j.1749-6632.1991.tb17013.x.

127. Mehra, A. Kaur, G., Sethi, S., Kumar, P., Bhandari, T., Kaur, K. et al. (2024) ‘Unveiling the potential of Bakuchiol-a comprehensive review on pharmacological activities and therapeutic formulations’, Journal of Biologically Active Products from Nature, 14(2), pp. 134–160.

doi:10.1080/22311866.2024.2346348.

128. Milosheska, D. and Roškar, R. (2022) ‘Use of retinoids in topical antiageing treatments: A focused review of clinical evidence for conventional and nanoformulations’, Advances in Therapy, 39(12), pp. 5351–5375. doi:10.1007/s12325-022-02319-7.

129. Mukherjee, S., Date, A., Patravale, V., Korting, H.C., Roeder, A., Weindl, G. (2006) ‘Retinoids in the treatment of Skin ageing: An overview of clinical efficacy and safety’, Clinical Interventions in Ageing, 1(4), pp. 327–348. doi:10.2147/ciia.2006.1.4.327.

130. Nabi, N.G. and Shrivastava, M. (2017) ‘Endangered medicinal Plant Psoraa corylifolia: Traditional, phytochemical, therapeutic properties and micropropagation’, Pharmaceutical and Biosciences Journal, pp. 40–46. doi:10.20510/ukjpb/5/i1/147024.

131. Officer, D. (2023) ‘UK facial skincare format & ingredient trends market report 2023’ Mintel Store. Available at: https://store.mintel.com/report/uk-facial-skincare-format-and-ingredient-trends-market-report

132. Panchal, V.S., Patel, Y.S., Dalal, Y.D., Parikh, A.P., Dalal, A.D., Rana, D.A. (2023) ‘Efficacy of oral, topical, and intradermal tranexamic acid in patients with Melasma — a meta-analysis’, Indian Dermatology Online Journal, 15(1), pp. 55–63. doi:10.4103/idoj.idoj_495_22.

133. Park, S.J. (2022) Chemical structures of bakuchiol (top) and retinol (bottom). Bakuchiol and retinol do not share structural similarity., A comprehensive review of topical bakuchiol for the treatment ofphotoageing. Journal of Integrative Dermatology. Available at: https://www.researchgate.net/publication/367052005_A_Comprehensive_Review_of_Topical_Bakuchiol_for_the_Treatment_of_Photoageing (Accessed: August 2025).

134. Pasquali-Ronchetti, I. and Baccarani-Contri, M. (1997) ‘Elastic fiber during development and ageing’, Microscopy Research and Technique, 38(4), pp. 428–435. doi:10.1002/(sici)1097-0029(19970815)38:4<428::aid

-jemt10>3.0.co;2-l.

135. Pfaller, M. A., Diekema, D. J., Mendez, M., Kibbler, C., Erzsebet, P., Chang, S. C., Gibbs, D. L., and Newell, V. A.et al. (2006) ‘Candida guilliermondii, an opportunistic fungal pathogen with decreased susceptibility to fluconazole: Geographic and temporal trends from the Artemis Disk Antifungal Surveillance Program’, Journal of Clinical Microbiology, 44(10), pp. 3551–3556. doi:10.1128/jcm.00865-06.

136. Polakova, K, Fauger A, Sayag M, Jourdan E. Jourdan, E. (2015) ‘A dermocosmetic containing bakuchiol, ginkgo biloba extract and mannitol improves the efficacy of adapalene in patients with acne vulgaris: Result from a controlled randomized trial’, Clinical, Cosmetic and Investigational Dermatology, p. 187. doi:10.2147/ccid.s81691.

137. Poon, F., Kang, S. and Chien, A.L. (2014) ‘Mechanisms and treatments of photoageing’, Photodermatology, Photoimmunology &; Photomedicine, 31(2), pp. 65–74. doi:10.1111/phpp.12145.

138. Prockop, D.J. (1982) ‘How does a skin fibroblast make type I collagen fibers?’, Journal of Investigative Dermatology, 79(1), pp. 3–6. doi:10.1038/jid.1982.2.

139. Putriana, N.A., Husni, P. and Mita, S.R. (2024) Recent advance Bakuchiol application as a potential alternative to retinol in skincare and cosmetics [Preprint]. doi:10.20944/preprints202401.1378.v1.

140. Quan, T., He, T., Kang, S., Voorhees, J.J., Fisher, G.J. et al. (2002) ‘Ultraviolet irradiation alters transforming growth factor β/SMAD pathway in human skin in vivo’, Journal of Investigative Dermatology, 119(2), pp. 499–506. doi:10.1046/j.1523-1747.2002.01834.x.

141. Quan, T., Little, E., Quan, H., Qin, Z., Voorhees, J.J., Fisher, G.J. (2013) ‘Elevated matrix metalloproteinases and collagen fragmentation in photodamaged human skin: Impact of altered extracellular matrix microenvironment on dermal fibroblast function’, Journal of Investigative

Dermatology, 133(5), pp. 1362–1366. doi:10.1038/jid.2012.509.

142. Quan, T., Qin, Z., Xia, W., Shao, Y., Voorhees, J.J., Fisher, G.J. (2009) 'Matrix-degrading metalloproteinases in photoageing', Journal of Investigative Dermatology Symposium Proceedings, 14(1), pp. 20–24. doi:10.1038/jidsymp.2009.8.

143. Quan, T., Qin, Z., Xu, Y., He, T., Kang, S., Voorhees, J.J., Fisher, G.J. (2010) 'Ultraviolet irradiation induces cyr61/CCN1, a mediator of collagen homeostasis, through activation of transcription factor AP-1 in human skin fibroblasts', Journal of Investigative Dermatology, 130(6), pp. 1697 –1706. doi:10.1038/jid.2010.29.

144. Quan, T., Shao, Y., He, T., Voorhees, J.J., Fisher, G.J., (2010) 'Reduced expression of connective tissue growth factor (CTGF/CCN2) mediates collagen loss in chronologically aged human skin', Journal of Investigative Dermatology, 130(2), pp. 415–424.doi:10.1038/jid.2009.224.

145. Qin, Z., Balimunkwe, R.M. and Quan, T. (2017) 'Age-related reduction of dermal fibroblast size upregulates multiple matrix metalloproteinases as observed in aged human skin in vivo', British Journal of Dermatology, 177(5), pp. 1337–1348. doi:10.1111/bjd.15379.

146. Raghow, R, Postlethwaite, A.E., Keski-Oja, J., Moses, H.L., Kang, A.H. (1987) 'Transforming growth factor-beta increases steady state levels of type I procollagen and fibronectin messenger RNAS post transcriptionally in cultured human dermal fibroblasts.', Journal of Clinical Investigation, 79(4), pp. 1285–1288. doi:10.1172/jci112950.

147. Rastogi, R.P., Richa, Kumar, A., Tyagi, M.B., Sinha, R.P. Rastogi, R. (2010) 'Molecular mechanisms of ultraviolet radiation-induced DNA damage and Repair', Journal of Nucleic Acids, 2010(1). doi:10.4061/2010/592980.

148. Ravanat, J.-L., Douki, T. and Cadet, J. (2001) 'Direct and indirect effects of UV radiation on DNA and its components', Journal of Photochemistry

and Photobiology B: Biology, 63(1–3), pp. 88–102. doi:10.1016/s1011-1344(01)00206-8.

149. Rezaee, Z.., Tsui, J., Cheng, P., Zhou, G. (2019a) ‘Ethical Dimension of Sustainability’, in Business Sustainability in Asia: Compliance, Performance, and Integrated Reporting and Assurance. First. John Wiley & Sons, Inc., pp. 263–288.

150. Rezaee, Z. Tsui, J., Cheng, P., Zhou, G (2019b) ‘Introduction to Business Sustainability’, in Business Sustainability in Asia: Compliance, Performance, and Integrated Reporting And Assurance. First. John Wiley & Sons, Inc., pp. 1–19.

151. Rijken, F. and Bruijnzeel, P.L. (2009) ‘The pathogenesis of photoageing: The role of neutrophils and neutrophil-derived enzymes’, Journal of Investigative Dermatology Symposium Proceedings, 14(1), pp. 67–72. doi:10.1038/jidsymp.2009.15.

152. Rijken, F., Bruijnzeel, P.L., van Weelden, H. (2007) “The Glycation Pattern of Aged Collagen in Human Skin and its Relationship to Yellowing,” Journal of Investigative Dermatology, 127, pp.2646–2654.

153. Rittie, L. and Fisher, G.J. (2002) ‘UV-light-induced signal cascades and skin ageing’, Ageing Research Reviews, 1(4), pp. 705–720. doi:10.1016/s1568-1637(02)00024-7.

154. Rittie, L., Kang, S., Voorhees, J.J., Fisher, G.J. (2008) ‘Induction of collagen by estradiol’, Archives of Dermatology, 144(9).doi:10.1001/archderm.144.9.1129.

155. Rohini, R. and Meppurath, D. (2024) ‘Dimensions of ethical consumption: a systematic review and Future Outlook’, Sustainable Development, 33(2), pp. 1892–1908. doi:10.1002/sd.3225.

156. Roig-Rosello, E. and Rousselle, P. (2020) Graphical Abstract, The Human Epidermal Basement Membrane: A Shaped and Cell Instructive Platform That Ageing Slowly Alters. Biomolecules. Available at: https://doi.org/10.3390/biom10121607 (Accessed: August 2025).

157. Rossetti, D., Kielmanowicz M.G., Vigodman S., Hu Y.P., Chen N., Nkengne A., Oddos T., Fischer D., Seiberg M., Lin C.B. (2011) 'A novel anti -ageing mechanism for retinol: Induction of dermal elastin synthesis and Elastin Fibre Formation', International Journal of Cosmetic Science, 33(1), pp. 62–69. doi:10.1111/j.1468-2494.2010.00588.x.

158. Ryu, J., Park, S.J., Kim, I.H., Choi, Y.H. and Nam, T.J. (2014) 'Protective effect of porphyra-334 on UVA-induced photoageing in human skin fibroblasts', International Journal of Molecular Medicine, 34(3), pp. 796 –803. doi:10.3892/ijmm.2014.1815.

159. Sakai, L.Y., Keene, D.R. and Engvall, E. (1986) 'Fibrillin, a new 350-KD glycoprotein, is a component of extracellular microfibrils.', The Journal of cell biology, 103(6), pp. 2499–2509. doi:10.1083/jcb.103.6.2499.

160. Sato, K., Morita, M., Ichikawa, C., Takhaski, H., Toriyama, M. et al. (2008) 'Depigmenting mechanisms of all-trans RA and retinol on B16 Melanoma Cells', Bioscience, Biotechnology, and Biochemistry, 72(10), pp. 2589–2597. doi:10.1271/bbb.80279.

161. Scharfetter-Kochanek, K., Brenneisen, P., Wenk, J., Herrmann, G., Ma, W., Kuhr, L., Meewes, C., Wlaschek, M. (2000) 'Photoageing of the skin from phenotype to mechanisms', Experimental Gerontology, 35(3), pp. 307 –316. doi:10.1016/s0531-5565(00)00098-x.

162. Schmidt, J.B., Binder, M., Demschik, G., Bieglmayer, C., Reiner, A. (1997) 'Treatment of skin ageing with topical estrogens', International Journal of Dermatology, 35(9), pp. 669–674. doi:10.1111/j.1365-4362.1996.tb03701.x.

163. Schwartz, E. and Kligman, L.H. (1995) 'Topical tretinoin increases the tropoelastin and fibronectin content of photoaged hairless mouse skin', Journal of Investigative Dermatology, 104(4), pp. 518–522. doi:10.1111/1523-1747.ep12606007.

164. Schurer, N.Y. and Elias, P.M. (1991) 'The biochemistry and function of SC lipids', Advances in Lipid Research, pp. 27–56. doi:10.1016/b978-0-12-024924-4.50006-7.

165. Shahzad, M.F. Yuan, J., Shahzad, K., Huang, Y. (2024) 'Drivers of Green Consumption: Ethical ideologies and corporate social responsibility in Sustainability Awareness', Sustainable Development [Preprint]. doi:10.1002/sd.3238.

166. Shao, Y., He, T., Fisher, G.J., Voorhees, J.J., Quan, T. et al. (2016) 'Molecular basis of retinol anti-ageing properties in naturally aged human skin in vivo', International Journal of Cosmetic Science, 39(1), pp. 56–65. doi:10.1111/ics.12348.

167. Sherratt, M.J. (2013) 'Age-related tissue stiffening: Cause and effect', Advances in Wound Care, 2(1), pp. 11–17.doi:10.1089/wound.2011.0328.

168. Sherber, N. (2018). The Millennial Mindset. Journal of drugs in dermatology : JDD, 17(12), 1340–1342.

169. Shimizu, T. (2005) 'Role of macrophage migration inhibitory factor (MIF) in the skin', Journal of Dermatological Science, 37(2), pp. 65–73. doi:10.1016/j.jdermsci.2004.08.007.

170. Shu, P., Li, M., Zhao, N., Wang, Y., Zhang, L., Du, Z. (2023) 'Efficacy and mechanism of retinyl palmitate against UVB-induced skin photoageing', Frontiers in Pharmacology, 14. doi:10.3389/fphar.2023.1278838.

171. Shu, P. Li, M., Li, Y., Yuan, Z., Lin, L., Wen, J. Aisa, H., Du, Z. (2023) 'Comparison of five retinoids for anti-photoageing therapy: Evaluation of anti-inflammatory and anti-oxidative activities *in vitro* and therapeutic efficacy in vivo', Photochemistry and Photobiology, 100(3), pp. 633–645. doi:10.1111/php.13872.

172. Sofen, B., Prado, G., and Emer, J. (2016). Melasma and Post Inflammatory Hyperpigmentation: Management Update and Expert Opinion. Skin therapy letter, 21(1), 1–7. PMID:27224897.

173. Sołdacka, D., Podgórska, M. and Barańska-Rybak, W. (2023) 'Unique retinol therapy with antioxidant and anti-inflammageing complex for naturally reborn skin: The clinical case series study', Dermatologic Therapy, 2023(1). doi:10.1155/2023/5588525.

174. Son, H., Kim, N., Song, CH., Lee, S.M., Lee, H.N., Surh, Y.J. Son, H.J. (2020) '17β-estradiol reduces inflammation and modulates antioxidant enzymes in colonic epithelial cells', *The Korean Journal of Internal Medicine*, 35(2), pp. 310–319. doi:10.3904/kjim.2018.098

175. Sorg, O., Antille, C., Kaya, G, Saurat, J.H. (2006) 'Retinoids in Cosmeceuticals', *Dermatologic Therapy*, 19(5), pp. 289–296. doi:10.1111/j.1529-8019.2006.00086.x.

176. Stanczyk, F.Z. (2009) 'Production, clearance, and measurement of steroid hormones', *The Global Library of Women's Medicine* [Preprint]. doi:10.3843/glowm.10278.

177. Sugawara, T., Iwamoto, N., Akashi, M., Kojima, T., Hisatsune, J., Sugai, M., Furuse, M. (2013) 'Tight junction dysfunction in the stratum granulosum leads to aberrant SC barrier function in claudin-1-deficient mice', *Journal of Dermatological Science*, 70(1), pp. 12–18. doi:10.1016/j.jdermsci.2013.01.002.

178. Szymański, Ł., Skopek, R., Palusińska, M., Schenk, T., Stengel, S., Lewicki, S., Kraj, L., Kamiński, P. Zelent, A. *et al.* (2020) 'RA and its derivatives in skin', *Cells*, 9(12), p. 2660. doi:10.3390/cells9122660.

179. Tan, J., Tan, F.J. and Ramakrishna, S. (2022) 'Transitioning to a circular economy: A

systematic review of its drivers and barriers', *Sustainability*, 14(3), p. 1757. doi:10.3390/su14031757.

180. Tajima, S., Hayashi, A. and Suzuki, T. (1997) 'Elastin expression is up -regulated by RA but not by retinol in chick embryonic skin fibroblasts', *Journal of Dermatological Science*, 15(3), pp. 166–172. doi:10.1016/s0923-1811(97)00598-7.

181. Temova Rakuša, Ž., Škufca, P., Kristl, A., Roškar, R. (2020) 'Quality Control of retinoids in commercial cosmetic products', *Journal of Cosmetic Dermatology*, 20(4), pp. 1166–1175. doi:10.1111/jocd.13686.

182. Temova Rakuša, Ž., Škufca, P., Kristl, A., Roškar, R. (2020) 'Retinoid stability and degradation kinetics in commercial cosmetic products', *Journal of Cosmetic Dermatology*, 20(7), pp. 2350–2358. doi:10.1111/jocd.13852.

183. *The 17 goals | sustainable development (2015) United Nations. Available at: https://sdgs.un.org/goals (Accessed: 22 May 2025).*

184. Trompezinski, S., Weber, S., Cadars, B., Larue, F., Ardiet, N., Chavagnac-Bonneville, M., Sayag, M., Jourdan, E. (2016). Assessment of a new biological complex efficacy on dysseborrhea, inflammation, and Propionibacterium acnes proliferation. *Clinical, cosmetic and investigational dermatology*, *9*, 233–239.doi:10.2147/CCID.S110655

185. Varani, J., Dame, M.K., Rittie, L., Fligiel, S.E., Kang, S., Fisher, G.J., and Voorhees, J.J. (2006) 'Decreased collagen production in chronologically aged skin', The American Journal of Pathology, 168(6), pp. 1861–1868. doi:10.2353/ajpath.2006.051302.

186. Varani, J., Perone, P., Warner, R.L., Dame, M.K., Kang, S., Fisher, G.J., Voorhees, J.J. Varani, J. et al. (2008) 'Vascular tube formation on matrix metalloproteinase-1-damaged collagen', British Journal of Cancer, 98(10), pp. 1646–1652. doi:10.1038/sj.bjc.6604357.

187. Varani, J., Warner, R.L, Gharaee-Kermani M., Phan, S.H., Kang, S., Chung, J.H., Wang, Z.Q., Datta, S., Fisher, G.J., Voorhees, J.J. (2000) 'Vitamin A antagonizes decreased cell growth and elevated collagen-degrading matrix metalloproteinases and stimulates collagen accumulation in naturally aged human skin1', Journal of Investigative Dermatology, 114(3), pp. 480–486. doi:10.1046/j.1523-1747.2000.00902.x.

188. Varga, J., Rosenbloom, J. and Jimenez, S.A. (1987) 'Transforming growth factor β (TGFβ) causes a persistent increase in steady-state amounts of type I and type III collagen and fibronectin mrnas in normal human dermal fibroblasts', Biochemical Journal, 247(3), pp. 597–604. doi:10.1042/bj2470597.

189. Vivat-Hannah, V. and Zusi, F. (2005) 'Retinoids as therapeutic agents: Today and Tomorrow', Mini-Reviews in Medicinal Chemistry, 5(8), pp. 755 –760. doi:10.2174/1389557054553820.

190. Waller, J.M. and Maibach, H.I. (2005) 'Age and skin structure and function, a quantitative approach (i): Blood flow, ph, thickness, and ultrasound echogenicity', Skin Research and Technology, 11(4), pp. 221–235. doi:10.1111/j.0909-725x.2005.00151.x.

191. Wang, J.V. et al. (2019) 'Patient perception of beauty on social media: Professional and bioethical obligations in esthetics', Journal of Cosmetic Dermatology, 19(5), pp. 1129–1130. doi:10.1111/jocd.13118.

192. Watson, R.E.B., Gibbs, N. K., Griffiths, C.E.M. and Sherratt, M.J. (2014) 'Damage to skin extracellular matrix induced by UV exposure', Antioxidants & Redox Signaling, 21(7), pp. 1063–1077. doi:10.1089/ars.2013.5653.

193. Watson, R. E.B., Newton, V. L., Mcconnell, J. C., Hibbert, S. A., Graham, H. K., & (2015). Skin ageing: molecular pathology, dermal remodelling and the imageing revolution. Giornale italiano di dermatologia e venereologia organo ufficiale, Societa italiana di dermatologia e sifilografia, 150(6),

665–674.

194. Weihermann, A.C., Lorencini, M., Brohem, C.A., de Carvalho C.M. (2016) ‘Elastin structure and its involvement in skin photoageing’, International Journal of Cosmetic Science, 39(3), pp. 241–247. doi:10.1111/ics.12372.

195. Werb, Z., Banda, M.J., McKerrow, J.H. and Sandhaus, R.A. Werb, Z. (1982) ‘Elastases and elastin degradation.’, Journal of Investigative Dermatology, 79(s1). doi:10.1111/1523-1747.ep12546056.

196. Williams, A.L., Pace, N.D. and DeSesso, J.M. (2020) ‘Teratogen update: Topical use and third-generation retinoids’, Birth Defects Research, 112(15), pp. 1105–1114. doi:10.1002/bdr2.1745.

197. Yaar, M., Eller, M.S. and Gilchrest, B.A. (2002) ‘Fifty Years of Skin Ageing’, Journal of Investigative Dermatology Symposium Proceedings, 7(1), pp. 51–58. doi:10.1046/j.1523-1747.2002.19636.x.

198. Yaar, M. and Gilchrest, B.A. (2007) ‘Photoageing: Mechanism, prevention and therapy’, British Journal of Dermatology, 157(5), pp. 874–887. doi:10.1111/j.1365-2133.2007.08108.x.

199. Ye, Y., Li, Y., Xu, C., Wei, X. et al. (2023) ‘Improvement of mild photoaged facial skin in middle-aged Chinese females by a supramolecular retinol plus acetyl hexapeptide-1 containing essence’, Skin Health and Disease, 3(4). doi:10.1002/ski2.239.

200. Yin, S., Fan, C. Q., Wang, Y., Dong, L., & Yue, J. M. (2004). Antibacterial prenylflavone derivatives from Psoralea corylifolia, and their structure -activity relationship study. Bioorganic & medicinal chemistry, 12(16), 4387–4392. doi:10.1002/chin.200448184.

201. Yin, S., Luo, J., Qian, A., Du, J., Yang, Q., Zhou, S., Yu, W., Du, G., Clark, R.B., Walters, Carlton, S.M., Hu, H. (2013) ‘Retinoids activate the irritant

receptor TRPV1 and produce sensory hypersensitivity', Journal of Clinical Investigation, 123(9), pp. 3941–3951. doi:10.1172/jci66413.

202. Zane, D.M., Irwin, J.R. and Reczek, R.W. (2015) 'Do less ethical consumers denigrate more ethical consumers? the effect of willful ignorance on judgments of others', Journal of Consumer Psychology, 26(3), pp. 337–349. doi:10.1016/j.jcps.2015.10.002.

203. Zasada, M. and Budzisz, E. (2019) 'Retinoids: Active molecules influencing skin structure formation in cosmetic and dermatological treatments', Advances in Dermatology and Allergology, 36(4), pp. 392–397. doi:10.5114/ada.2019.87443.

204. Zhang, H., Apfelroth, S.D., Hu, W. Davis, E.C., Sanguineti, C., Bonadio, J., Mecham, R.P, Ramirez, F. (1994) 'Structure and expression of fibrillin-2, a novel microfibrillar component preferentially located in elastic matrices', The Journal of cell biology, 124(5), pp. 855–863. doi:10.1083/jcb.124.5.855.

205. Zhong, X., Deng, Y., Yang, H., Du, X., Liu, P., Du, Y. (2024) 'Role of autophagy in skin photoageing: A narrative review', Medicine, 103(8). doi:10.1097/md.0000000000037178.

206. Zouboulis, C.C. and Makrantonaki, E. (2012) 'Hormonal therapy of intrinsic ageing', Rejuvenation Research, 15(3), pp. 302–312. doi:10.1089/rej.2011.1249.

207. Zouboulis, C.C., (2003) 'Intrinsic skin ageing. A critical appraisal of the role of hormones],' Hautarzt, 54(9): pp. 825–832. doi:10.1007/s00105-0030581-7.