Australasian Society of Cosmetic Dermatologists

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OPINIONS AND PROGRESS IN Cosmetic Dermatology

VOLUME 04 / ISSUE 02 / FEBRUARY 2025

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COSMECEUTICALS

Welcome to the Cosmeceuticals Issue, our much-anticipated 10th edition since OPCD's launch in December 2020. This milestone not only celebrates our fifth year but also highlights the growing expertise within our editorial team.

We are thrilled to introduce three talented associate editors: Dr. Aakriti Gupta, Dr. Sarah Hannam, and Dr. Shreya Andric. As regular contributors to OPCD and ASCD conferences and education programs, they bring fresh perspectives to our editorial team.

The associate editors and I will rotate as co-editors-in-chief, each adding unique insights to every issue. Dr. Sarah Hannam, serving as co-editor-in-chief for this issue, brings a rich background in both medical and cosmetic dermatology. Her dedication to patient-centred care and evidence-based practice has been invaluable to this issue.

This issue also features guest editor Dr. Aakriti Gupta, an Adelaide cosmetic dermatologist, subspecialising in laser and cosmetic dermatology and hair disorders. Dr. Gupta was awarded the University Medal in Medicine from the University of Adelaide and completed a specialty dermatology fellowship in Oxford, UK. Dr. Gupta is also a board member of the Australasian Society of Cosmetic Dermatologists and an Editorial Board member of OPCD, making her a great choice to guide this issue.

Following the success of Tradescraft 1 (Issue 9), we return with a more traditional journal format, focusing on the ever-relevant field of cosmeceuticals. Dermatologists are increasingly asked, "Doctor, what skincare products do you recommend?" This Cosmeceutical issue aims to support clinicians in responding with the latest evidence-based insights and expert guidance for better patient care.

As always, OPCD is here to support your educational journey, and we welcome your feedback on how we can continue to meet your professional needs. As 2025 unfolds, we hope you enjoy this issue and look forward to seeing you at the Melbourne ASCD conference this March.

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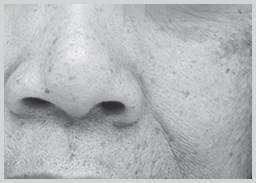
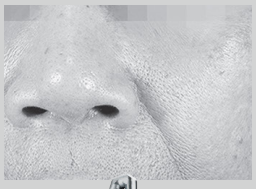
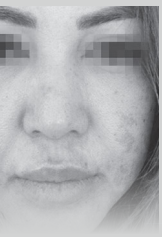
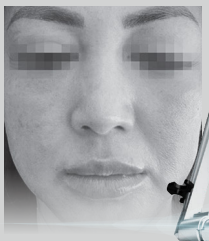

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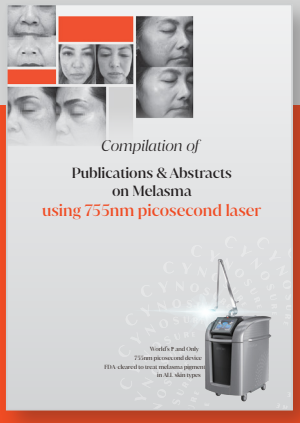
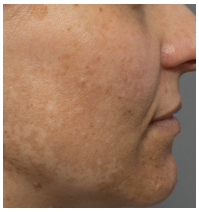
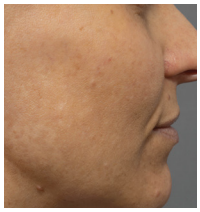
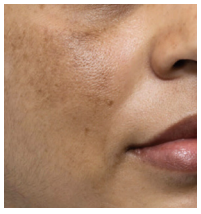
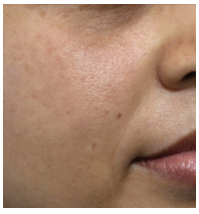


Download our Compilation of Publications & Abstracts on Melasma using 755nm Picosecond Laser

2x TX sessions of PicoSure for Melasma
Courtesy of Lotus Hansford, Cutis Dermatology

4x TX sessions of PicoSure for Melasma
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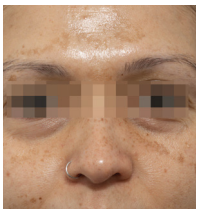
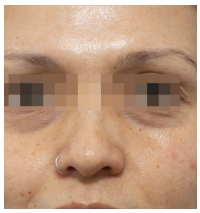
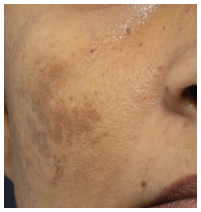
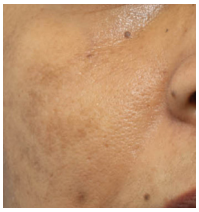



3x TX sessions of PicoSure for Melasma
Courtesy of Lara, Cutis Dermatology

4x TX sessions of PicoSure for Melasma
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Guest Editorial
Cosmeceuticals – The Science Behind Modern Skincare

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Gupta A. Guest editorial. Opin Prog Cosmet Dermatol. 2025;4(2):1.

Cosmeceuticals, a subset of cosmetic products that aim to provide targeted solutions for specific skin concerns, have revolutionised the world of skincare.

With patients increasingly seeking science-backed solutions, dermatologists must navigate this expanding field to recommend effective, evidence-based products.

This special issue offers diverse perspectives on cosmeceuticals, bringing together experts to explore innovations, challenges, and future directions in this space.

Highlights from this issue include:

Michelle Rodrigues and Samuel Morriss tackle *pigmentation disorders*, reviewing active ingredients like niacinamide, arbutin, and tranexamic acid, and thoroughly evaluate the evidence for these actives.

Jo-Ann See and Kate DeAmbrosis provide insights into *cosmeceuticals for acne* and discuss how these can be integrated into acne treatment protocols to optimise patient outcomes.

Shobhan Manoharan and Piyu Naik examine *advances in topical antioxidants*, with a focus on combating oxidative stress from UV exposure and pollution. They discuss established and emerging antioxidants including vitamin C, resveratrol and coenzyme Q10.

I ask the question, '*Is there an ideal skincare routine?*' and aim to debunk many of the common myths and misconceptions with regards to skincare.

Michelle Wong and Hannah English explore the latest *trends in cosmeceutical ingredients*, focusing on mechanistic plausibility and credibility of evidence.

Terri (Vinson) Jones contributes two articles: one on *peptides, growth factor & exosomes*, explaining how these can impact skin properties through cell signalling, and another on *nutraceuticals*, which focuses on dietary supplements that support skin health from within.

Katherine Armour discusses *social media's impact on skincare trends*. With platforms like Instagram and TikTok influencing consumer behaviour, Armour emphasises the importance of dermatologists guiding patients toward evidence-based products amidst misinformation.

Patricia Lowe and Michelle Wu introduce readers to *nanotechnology in cosmetic dermatology*, exploring how nanoscale formulations improve ingredient delivery, enhance efficacy, and overcome challenges associated with stability and absorption.

Additionally, Sarah Hannam, Shreya Andric, and Des Gan reveal their *favourite cosmeceutical ingredients*, offering personal insights into what works best in practice.

This issue offers a comprehensive look at cosmeceuticals, from the latest scientific innovations to the influence of social media and personal recommendations from experts.

I hope this collection of articles sparks discussion, new research and improves the 'prescribing' of cosmeceuticals in Dermatology.

Dr Aakriti Gupta

Cosmeceuticals for Hyperpigmentation

Samuel Morriss[1,2], Michelle Rodrigues[3]

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Disclosures: *None.*

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OUTLINE: Hyperpigmentation encompasses a broad spectrum of conditions, ranging from lentigines to refractory melasma, necessitating accurate diagnosis for effective management. Cosmeceuticals, defined as products that bridge cosmetics and pharmaceuticals by offering therapeutic benefits, have emerged as adjuncts in managing hyperpigmentation, particularly melasma and post-inflammatory hyperpigmentation (PIH). Despite their popularity, cosmeceuticals are not yet formally recognised by regulatory bodies, and there is limited robust evidence regarding their efficacy.

This review outlines the evidence landscape of various cosmeceuticals used in hyperpigmentation. Azelaic acid, kojic acid, and arbutin can effectively treat conditions such as melasma and PIH. However, the effectiveness of cosmeceuticals is often constrained by formulation instability and poor skin penetration. This article explores novel formulations and drug delivery systems to enhance drug penetration.

Given the limited evidence in this field, it is imperative that clinicians objectively evaluate the literature and guide patients based on evidence-based recommendations. Robustly designed studies using validated outcome measures are needed to better assess the safety and efficacy of these agents.

KEYWORDS: hyperpigmentation, melasma, cosmeceuticals, post-inflammatory hyperpigmentation, skin of colour

Morriss S and Rodrigues M. Cosmeceutials for hyperpigmentation. Opin Prog Cosmet Dermatol. 2025;4(2):2–9.

Introduction

Cosmeceuticals are often used to manage hyperpigmentary disorders. However, studies often refer to 'hyperpigmentation' as an umbrella term that includes everything from solar lentigines to refractory melasma. With several dozen causes of hyperpigmentation on the face alone, making an accurate diagnosis is the critical first step in successful management. Each cause of hyperpigmentation requires a slightly different management approach that addresses the pathophysiology.

Melasma and post-inflammatory hyperpigmentation (PIH) are the most common hyperpigmentary conditions. In many cases, trials of various topical therapies alongside photoprotection are required.[1,2] As such, this article will focus on using cosmeceuticals to manage these two conditions.

The term 'cosmeceuticals' was first introduced in 1984 to describe products that go beyond purely cosmetic applications and have a pharmaceutically therapeutic effect.[3] Cosmeceuticals are not formally recognised by the United States Food and Drug Administration[4] or the Australian Therapeutic Goods Administration[5] despite this category of skin care products being reported in the literature and sold commercially for years. Whilst many cosmeceuticals exist to address hyperpigmentation, the lack of regulation and formal consensus regarding these products has resulted in studies that lack solid methodology and use of validated outcome measures. Meaningful insights into the safety and efficacy of these agents, particularly for treating pigmentary disorders like melasma and PIH, are thus scarce. This review will outline the evidence landscape of cosmeceuticals for treating melasma and PIH from oldest to newest agent (also summarised in Table 1).

Table 1. *An overview of cosmeceuticals that are available to treat melasma and post-inflammatory hyperpigmentation (PIH).*

Agent	Type of chemicals	Mechanism of action	Efficacy in melasma	Efficacy in PIH	Key points
Azelaic Acid	Dicarboxylic acid from *Malasezzia spp.*	Inhibits tyrosinase, reduces DNA synthesis in melanocytes, anti-inflammatory, antioxidant	Effective in melasma as an alternative or adjunct to hydroquinone	Effective in post-acne PIH	Concentrations reported in the literature range from 15–20% Mild adverse effects can be seen, but skin tolerance usually develops
Kojic Acid	Fungal metabolite	Inhibits tyrosinase, has copper-chelating, antioxidant properties	Effective as an adjunct, especially when used with glycolic acid or hydroquinone	Limited data	2% concentration reported Risk of skin sensitisation
Arbutin	Hydroquinone derivative	Tyrosinase inhibitor, antioxidant	Improvements in melasma with synthetic forms more effective (such as alpha- or deoxyarbutin)	Limited data	2.51% concentration reported Generally well-tolerated, occasional irritation
Ascorbic Acid	Vitamin C	Tyrosinase inhibitor, antioxidant	Comparable efficacy to HQ	Limited studies; some evidence in reducing post-acne hyperpigmentation in combination with HQ	Concentrations range from 10–20% Poor skin penetration requires delivery enhancement techniques Minimal side effects
Tranexamic Acid	Anti-plasmin molecule	Inhibits melanogenesis-promoting factors (eg. melanocyte-stimulating hormones, prostaglandins and kinins), inhibits histamine release from mast cells, antioxidant	Effective orally, variable efficacy topically depending on formulation	Limited data	Co-enhancing technology like microneedling may increase efficacy given its hydrophilic nature and poor epidermal penetration
Niacinamide	Vitamin B3 derivative	Inhibits melanosome transfer to keratinocytes	Effective as adjunct to arbutin, retinaldehyde, TXA, kojic acid and cysteamine in melasma treatment	Limited data	Concentrations reported 2–10%
Cysteamine	Aminothiol compound	Tyrosinase and peroxidase inhibition, glutathione upregulation thereby shifting melanin synthesis from eumelanin to pheomelanin	Effective in melasma, conflicting evidence in comparison to the efficacy of HQ	5% cysteamine demonstrates comparable efficacy to combination HQ/ ascorbic acid in post-acne PIH	Theoretical risk of UV-independent melanomagenesis by activation of the pheomelanin synthesis pathway, although no evidence currently supports this
Thiamidol	Resorcinyl thiazole derivative	Tyrosinase inhibitor	Comparable efficacy to hydroquinone	Variable efficacy, shown to reduce laser-induced PIH in some studies	0.1–0.2% concentration range Generally well-tolerated, contact dermatitis reported in few cases

Azelaic acid

Azelaic acid is a dicarboxylic acid found naturally in wheat produced by *Malasezzia spp*., the yeast responsible for pityriasis versicolor.[6] It acts as an anti-pigment agent through multiple mechanisms, including inhibiting tyrosinase,[7] inhibiting DNA synthesis and mitochondrial enzymes of hyperactive melanocytes,[8,9] and acting as an anti-inflammatory and antioxidant.[10] The most common regimen reported is the application of 20% azelaic acid twice daily.[11] A recent systematic review of six studies comparing azelaic acid to hydroquinone (HQ) for melasma found similar rates of side effects, including local irritation, itching, and scaling.[12] Azelaic acid may be a suitable alternative for those unable to tolerate HQ, for whom HQ is contraindicated (e.g., pregnant or breastfeeding women), or as an adjunct alongside other agents in refractory melasma.

A recent randomised controlled trial (RCT) compared the use of 15% azelaic acid gel and placebo in 72 patients with post-acne PIH. It found that azelaic acid reduced the post-acne hyperpigmentation index (PAHPI) by 6 points and increased patient satisfaction compared with the control. Although most participants experienced mild facial erythema, tingling, and dryness, skin tolerance to azelaic acid developed throughout the study.[13] The efficacy of the twice-daily application of a 15% azelaic acid gel was also seen in 20 skin-of-colour patients with moderate to severe post-acne PIH. At the end of the study, 100% of patients had at least a 2-point improvement in the investigator-graded assessment of their PIH. However, 20% of patients reported dry skin and peeling.[14]

Kojic acid

Kojic acid (KA), named after the fungi *Aspergillus oryzae*, also known as 'Koji', is a metabolic product of certain species of fungi, including *Aspergillus*, *Acetobacter*, and *Penicillum*.[15] It acts as a depigmenting agent by inhibiting tyrosinase.[15,16]

KA is most useful when combined with another depigmenting agent. In a split-face study, a 5% glycolic acid and 2% KA combination demonstrated superior efficacy in melasma compared with a 5% glycolic acid and 2% HQ formulation.[17] Other studies also corroborate these results,[18] suggesting that KA is a useful adjunct to glycolic acid and HQ for epidermal lightening in melasma.

As only two studies have assessed the efficacy of KA in PIH,[19,20] more work is needed. The frequency of KA-induced skin sensitisation ranges from 12–63%[18,21] which should be borne in mind.

Arbutin

Arbutin is a naturally occurring derivative of HQ found in the leaves of pear, bearberry, and cranberry plants. It acts as a tyrosinase inhibitor and antioxidant.[22,23] Arbutin is non-toxic to melanocytes and does not downregulate tyrosinase expression.[24]

An RCT of 102 women with melasma compared a 2.51% arbutin cream with a placebo. A total of 75.86% of patients showed a statistically significant 18% decrease in melanin levels after 8 weeks of application.[25]

Synthetic forms of arbutin, such as alpha-arbutin and deoxyarbutin, have a greater inhibitory effect on tyrosine than the naturally occurring form.[26] An RCT has shown that 2% deoxyarbutin has comparable depigmenting efficacy to 4% HQ (as measured by quantitative skin colour chromameter and mexameter analysis), with no side effects seen in the 59 patients treated with deoxyarbutin.[27]

More robustly constructed studies are required to inform clinicians about the use of arbutin. However, it appears to be well-tolerated, with only a few reported cases of erythema and urticaria.[25,28]

Ascorbic acid

Ascorbic acid, also known as vitamin C, is a depigmenting agent that acts topically by interacting with copper ions at the active sites of tyrosinase and inhibiting its activity.[29] It is also an antioxidant, preventing free radical-induced melanogenesis.[30]

A 2023 systematic review concluded that the skin-lightening effect of ascorbic acid on melasma is comparable to that of HQ. Most studies assessed the efficacy of ascorbic acid at a concentration of up to 10%, with one study assessing a concentration of 20%.[30]

However, ascorbic acid has a limited ability to penetrate the epidermis. Studies suggest it needs to be combined with laser and energy-based devices to induce clinically relevant changes in melasma and PIH.[31,32]

There is a paucity of well-constructed studies assessing ascorbic acid in PIH. A recent RCT of 30 patients comparing a 3% ascorbic acid/4% HQ cream to 5% cysteamine found a 2.90 reduction in mean PAHPI scores with the combination cream versus a mean PAHPI reduction of 2.41 with cysteamine alone.[33] No significant side effects have been reported in the literature.

Tranexamic acid

Tranexamic acid (TXA) is an anti-plasmin molecule that inhibits plasmin-derived production of kinins and other melanogenesis-promoting factors such as melanocyte-stimulating hormones.[34,35] It also inhibits histamine release from mast cells, which induces melanogenesis.[34]

The efficacy of oral TXA in melasma is well documented in the literature.[7,35] However, the hydrophilic nature of TXA applied topically limits its transdermal penetration and availability at melanocytes.[36,37] Studies have reported varying efficacy of different topical TXA formulations in melasma, which may be attributed to formulation-based differences in skin absorption.[37,38] Co-enhancing technology is required for this molecule to optimally penetrate the epidermis and robustly-constructed studies on these formulas are still lacking.[39]

Niacinamide

Niacinamide, or nicotinamide, is an amide form of vitamin B3 (niacin) that reversibly inhibits melanosome transfer to keratinocytes.[40] It does not inhibit tyrosinase or affect its expression.[40]

Most studies with statistically significant results use niacinamide in combination with other ingredients like arbutin, retinaldehyde, TXA and kojic acid to improve melasma.[19,41,42] Concentrations of 5–10% niacinamide are most commonly employed.

An RCT comparing a combination 2% niacinamide/2% TXA cream with a vehicle control in 42 women with facial hyperpigmentation showed a statistically significant decrease in mean melanin index from 131.16 to 119.62 at 8 weeks.[43] 4% niacinamide has also been paired with 2% N-acetyl glucosamine (NAG), where an RCT of 202 women with solar lentigines found greater reductions in melanin spot area with this combination compared with control.[44]

Other novel agents have been combined with niacinamide such as potassium azeloyl diglycinate, a derivative of azelaic acid. A combination of these two agents with TXA was assessed in an RCT, finding a 2.1-point reduction in Melasma Area and Severity Index (MASI) scores in 24 patients with mild to moderate melasma.[45] A novel phenylalanine-fatty acid derivative 1% N-undecylenoyl phenylalanine has also been shown to have efficacy in reducing hyperpigmentation in combination with niacinamide.[46] More recently, 5% niacinamide has been assessed in combination with 5% cysteamine, reporting improvement in MASI scores by 3.9 ± 2.3 in 35 patients with moderate to severe melasma.[47] In general, the literature supports niacinamide as a useful adjunct in the treatment of melasma.

The evidence for niacinamide in PIH is limited. One RCT assessed 24 women with PIH of the axilla and found that application of 4% niacinamide was associated with a >50% statistically significant improvement in pigmentation in 24% of patients.[48]

Cysteamine

Cysteamine is a naturally-occurring aminothiol derived from the degradation of coenzyme A.[49] It has been shown to inhibit tyrosinase and peroxidase,[50] and also upregulate intracellular glutathione causing a shift in eumelanin to pheomelanin production thereby slowing melanogenesis.[51,52] Cysteamine has only recently been stabilised in a hydrochloride compound to allow for development of suitable formulations.[49]

A systematic review of 6 studies concluded that 5% cysteamine is an effective treatment for melasma, with meta-analysis of the grouped studies reporting a 6.26 mean difference in modified MASI (mMASI) scores and minimal side effect profile.[53] Two RCTs have found cysteamine to be equally effective as the modified Kligman's Formula in melasma along with improved tolerability.[54,55]

There are confounding results in the literature surrounding the efficacy and tolerability of cysteamine compared with the gold-standard of HQ. One RCT reported similar reductions in mMASI compared with 4% HQ but more side effects were seen with 5% cysteamine.[56] However, another study showed an inferior performance in 5% cysteamine compared with 4% HQ (24% vs 41% reduction in mMASI scores respectively) but with similar rates of adverse effects including erythema and stinging.[57]

Another RCT divided 80 patients into receiving either 5% cysteamine or a combination 4% HQ/3% ascorbic acid cream. Comparable reductions in mMASI scores from both groups were noted after 4 months of treatment. However, 3 patients in the cysteamine group discontinued treatment due to erythema and pruritus.[58]

Few studies have assessed the role of cysteamine in PIH. As explored earlier in the discussion of ascorbic acid, 5% cysteamine has equivalent efficacy to 4% HQ/3% ascorbic acid in post-acne PIH.[33] Recently, cysteamine has been conjugated with isobionic-amide, a novel melanosome transfer inhibitor which is hypothesised to work synergistically with cysteamine in reducing skin pigmentation.[59]

Activation of the pheomelanin synthesis pathway results in oxidative damage and contributes to an ultraviolet-independent melanomagenesis pathway.[60] Due to the mechanism of cysteamine working to shift synthesis of eumelanin to pheomelanin, there is a theoretical risk of

developing melanoma with this agent. Nevertheless, to date no studies have demonstrated this association.

Thiamidol

The resorcinyl thiazole derivative thiamidol acts as a tyrosinase inhibitor.[61] The literature supports thiamidol as a useful depigmenting agent in melasma. A 4.2 ± 2.4 point improvement in MASI scores was cited in a 24-week RCT comparing thiamidol with a vehicle control in 51 patients with moderate to severe melasma.[62] Two RCTs have compared 0.2% thiamidol to 2% and 4% HQ in melasma, with both studies demonstrating comparable reductions in mMASI scores between the two agents.[63,64] Furthermore, one study substituted 5% HQ with 0.1% thiamidol found in the traditional triple combination (TCC) therapy Kligman's Trio (that also contains 0.1% dexamethasone and 0.1% tretinoin). The thiamidol-substituted group showed a greater 4.33-point improvement in mMASI scores versus a 2.84-point reduction in the TCC therapy group, although this difference was not statistically significant.[65]

There is variable evidence surrounding the use of thiamidol in PIH. In one study, 77 Fitzpatrick skin phototype V patients with post-acne PIH completed a 12-week RCT comparing thiamidol to a vehicle control finding a statistically significant reduction in melanin index scores.[66] Thiamidol has also been shown to reduce the incidence of Q-switched Nd:YAG laser-induced PIH with another RCT revealing twice-daily thiamidol may be helpful in reducing PIH incidence in this context.[67] Thiamidol appears to be well-tolerated in the literature with contact dermatitis reported in a minority of cases.[64,65]

Other cosmeceuticals: Soy, bakuchiol, and resveratrol

Soybean extract contains proteins such as soybean trypsin inhibitor that possesses serine protease inhibitor activity. These proteins inhibit protease-activated receptor 2, a key mediator involved in melanosome transfer and keratinocyte phagocytosis.[68,69] The extract also contains soy isoflavones which has antioxidant activity.[69] One study assessed the utility of a soy moisturiser in reducing photoaging, finding improvements in skin tone and texture along with a 25% improvement in mottled hyperpigmentation in the 65 participants compared with control.[70] Subtle skin lightening effects in treating solar lentigines have been reported, with one study citing a 15.1% reduction in melanin density with application of a stabilised soy extract.[71] Robustly constructed studies for the efficacy of soy in melasma and PIH are lacking.

Bakuchiol has been shown to evoke changes in gene expression similar to that of retinol.[72] Hence, most studies have assessed the efficacy of bakuchiol as an anti-aging compound.[72,73] A systematic review of 4 articles found mixed conclusions in the utility of bakuchiol in reducing post-acne PIH.[74] Overall, evidence for the use of bakuchiol specifically in hyperpigmentary conditions is sparse.

Although resveratrol has mainly been used for its anti-aging properties[75], it has gained attention for its potential use as a skin lightening agent. Resveratrol is claimed to reduce pigmentation through multiple actions including inhibition, downregulation, and post-transcriptional regulation of tyrosinase along with antioxidant effects.[76] Only one study has assessed the efficacy of topical resveratrol in humans.[77] Fifty healthy volunteers underwent UV-induced hyperpigmentation and lesions were subsequently treated with either 1% resveratrol, 1% resveratrol with an antioxidant, antioxidant alone or vehicle. The study found statistically significant reductions in melanin content with both resveratrol alone and resveratrol with antioxidant in comparison to vehicle. No robust studies have demonstrated efficacy in melasma.

Future directions

Azelaic acid, kojic acid, and arbutin have demonstrated efficacy in the treatment of conditions like melasma and PIH. The efficacy of many cosmeceuticals for hyperpigmentation appears to be limited by their stability, susceptibility to oxidative degradation, and poor penetrance through the epidermis. Novel formulations have been developed to improve the delivery of ascorbic acid, kojic acid, resveratrol, and arbutin by facilitating transdermal penetrance through the stratum corneum.[78,79]

Cosmeceuticals are increasingly popular in the treatment of hyperpigmentation, and many new cosmeceuticals are emerging in the market. Many ingredients claim efficacy for melasma and PIH but a closer look at the literature does not reveal robustly constructed studies using validated outcome measures. It is therefore imperative that the treating dermatologist objectively evaluates the merit of studies according to methodology, statistical significance, and outcome measures, and gives patients evidence-based recommendations.

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Cosmeceuticals for Acne

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CLICK IMAGE TO LINK TO VIDEO DURATION_00:30

Disclosures: Dr JoAnn See has received honoraria for speaking, writing educational material, and advisory board participation for Galderma, L'Oreal, Sun Pharma, Viatris, CSL Sequiris, and Mayne Pharma. Dr Kate DeAmbrosis has received honoraria for speaking, writing, and advisory board participation for L'Oreal.

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OUTLINE: Acne vulgaris is a common dermatological condition that affects a significant portion of the population, particularly during adolescence, with an incidence approximating 95% of boys and 85% of girls.1 Recently, an increasing prevalence of adult acne has been documented, with estimates of up to 35% of females affected.2 The pathogenesis of acne is multifactorial, involving a complex interplay of hyperactivity of the sebaceous gland, abnormal keratinisation, bacterial colonisation, and an altered microbiome, particularly involving Cutibacterium acnes (C. acnes), and inflammation. Acne can range from mild to severe, with potential long-term psychological impacts such as low self-esteem and depression due to scarring and physical appearance.

The management of acne vulgaris is multifaceted, often requiring a combination of pharmacological treatments, lifestyle modifications, and skincare regimens. In recent years, cosmeceuticals, i.e., products bridging the mechanistic effects of cosmetics and pharmaceuticals, have gained significant attention as adjunctive therapies in acne management. These products often contain bioactive ingredients that are intended not only to improve the cosmetic appearance of the skin but also to exert therapeutic effects on underlying skin conditions. They may play a role in managing mild acne, as well as maintenance therapy once the acne has cleared. They may also work synergistically with other acne treatments and enhance the efficacy and tolerability of prescription treatment, thus improving patient adherence to treatment.

We propose the increasing need for an evidence-based approach to this aspect of acne management. This approach would better tailor cosmeceutical ingredients to acne subtypes to improve overall efficacy, acne control, and skin maintenance long-term.

KEYWORDS: acne, cosmeceuticals, treatment, bioactives, synergy

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What are cosmeceuticals?

The term "cosmeceutical" was developed to describe products that have both cosmetic and therapeutic benefits. Unlike conventional cosmetics, which are primarily intended for beautification, cosmeceuticals contain active ingredients that influence the biological function of the skin. These ingredients are often derived from natural sources, such as plant extracts, vitamins, and minerals, but may also include synthetic compounds with known biological activities.

Cosmeceuticals are not classified as drugs and, therefore, do not require the same rigorous testing and approval process as pharmaceuticals. However, they are designed to exert effects beyond standard cosmetics, targeting specific skin concerns like acne, ageing, hyperpigmentation, and dryness.

The role of cosmeceutical agents in acne management[3]

- The role of cosmeceutical in acne control
- To maintain skin barrier function
- To maintain a healthy skin surface pH
- To maintain the skin microbiome diversity system

In acne, the skin barrier function can be compromised, which may lead to elevated sebum excretion and subclinical inflammation.[4] The overzealous use of both prescription and cosmeceutical agents can also exacerbate barrier dysfunction. Cosmeceutical ingredients such as panthenol, ceramides, glycerin and niacinamide can restore the skin barrier, thereby assisting effective acne management.

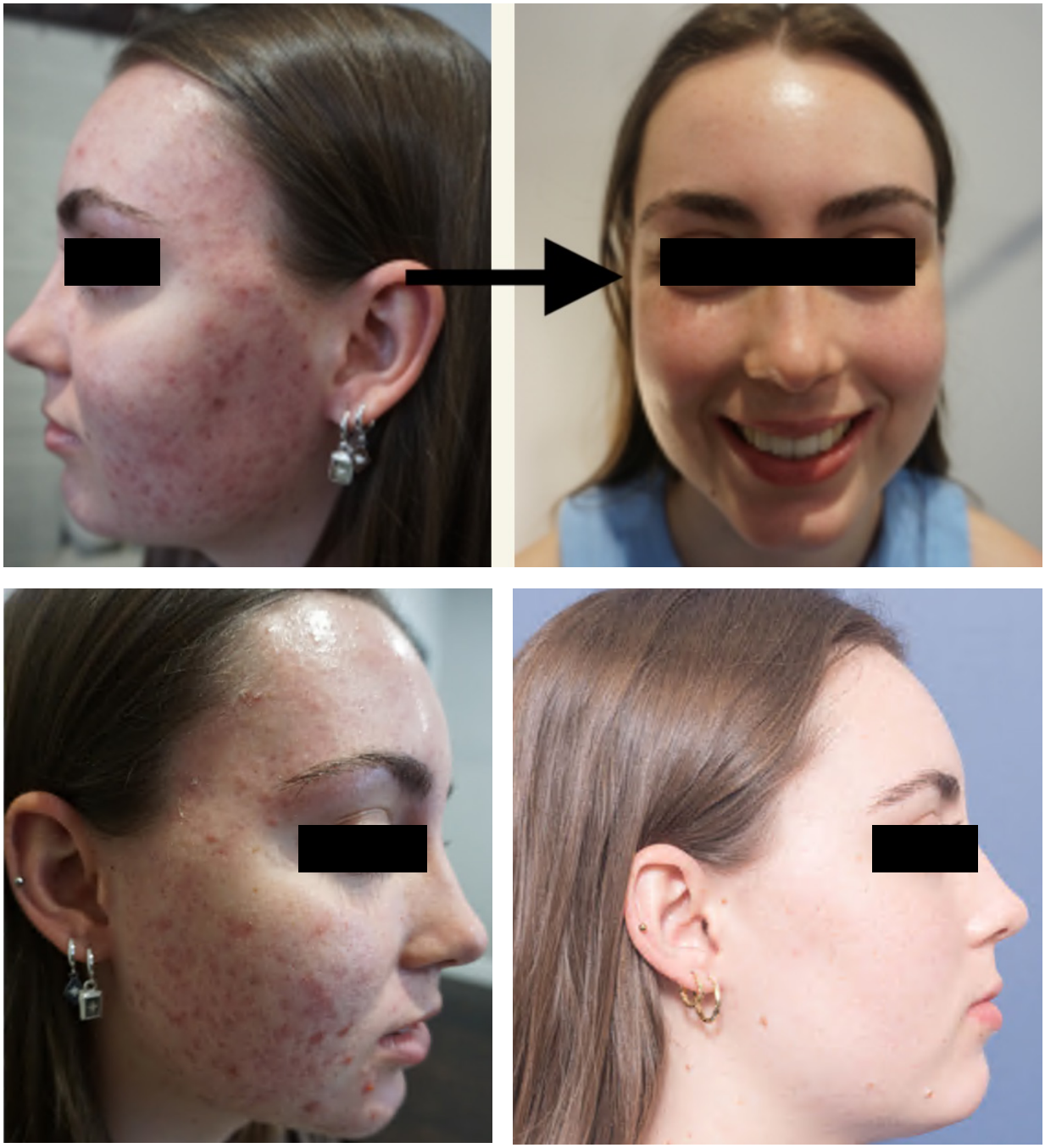

Figure 1. *This 19-year-old female with nodulocystic acne facial skin was treated for 12 months with a combined multimodal regime including oral low-dose isotretinoin 10 mg daily, a salicylic acid containing gel cleanser twice daily, a ceramide and pantheon containing emollient twice daily and regular adherence to sunscreen and photoprotective measures.*

The use of topical retinoids and benzoyl peroxide (BPO) has been associated with increased transepidermal water loss (TEWL), impaired permeability of the stratum corneum and increased sensitivity to UV radiation. This barrier alteration may be associated with side effects such as skin dryness, irritation, itching, flaking and peeling skin, and redness. Patients complain of these adverse effects, and this lack of tolerability often leads to poor adherence to treatment. This lack of adherence leads to poor treatment outcomes.[5]
A study of 596 dermatologists in 2015 demonstrated that cosmeceuticals were prescribed more consistently as an adjunct treatment for mild acne than severe acne, highlighting a potential gap in our therapeutic approach in moderate to severe acne.[6]

Cosmeceuticals may also normalise the skin surface pH, which may reduce Th2 inflammation and help normalise epidermal hyperproliferation. Cleansers and moisturisers should have a pH range of 4–6, resembling the physiological skin surface pH. This aims to prevent an increase in moisture vapour water loss and a change in protease-activated receptor 2 (PAR2), which affects skin barrier integrity and inflammation.

Table 1. *Cosmeceutical mechanism of action and impact on acne pathogenesis.*

Mechanism of action	Impact on acne pathogenesis	Example cosmeceutical ingredient
Anti-inflammatory effect	Reduced inflammation, skin erythema, pro-inflammatory cytokines, and oxidative stress.	Niacinamide (vitamin B3) Zinc Bakuchiol Panthenol
Sebum regulation	Overproduction, along with altered sebum viscosity, is a key contributor to acne-prone skin. Reduction in comedogenic free fatty acid levels and reduced sebum production levels minimise comedogenesis.	Zinc Niacinamide Bakuchiol Epigallocatechin-3-gallate
Antimicrobial action	The hyperproliferation of *C. acnes*, along with dysbiosis due to subtype diversity shifts among the eight phylotypes of these bacteria, contributes to the inflammatory component in acne. Beta-hydroxy acids (such as salicylic acid) are particularly effective in reducing pilosebaceous duct bacterial colonisation levels.	Salicylic acid Benzoyl peroxide Zinc *Lactobacillus plantarum*
Exfoliation and keratolysis	Abnormal keratinisation is a precursor to closed comedone formation.	AHAs (glycolic acid and lactic acid)
Antioxidant protection	Oxidative stress exacerbates inflammation and sebum oxidation, driving acne severity. These agents protect against oxidative damage.	Vitamin C Vitamin E Coenzyme Q10 Resveratrol

AHAs, alpha-hydroxy acids.

The altered microbiome in acne is characterised by a loss of diversity of *C. acnes* phylotypes, a predominance of 1 A1 type, and an increase of S. *epidermidis*. It is, therefore, vitally important to maintain a balanced skin microbiome on the skin surface and within the pilosebaceous unit. Probiotics may work in acne by inhibiting *C. acnes* growth or suppressing inflammation. *In vitro* studies have shown that they may release antimicrobial peptides, bacteriocin, or similar inhibitory substances that inhibit the growth of acne bacteria. They may also help restore the skin barrier and have immunomodulatory properties on keratinocytes that may inhibit the release of pro-inflammatory cytokines.[7]

A few clinical trials have assessed the effect of probiotic supplementation in patients with acne, indicating greater tolerance and compliance with oral antibiotics. One trial showed that probiotics decrease the adverse events associated with systemic antibiotics while providing synergistic benefits for inflammatory acne.[8]

The most used and best-studied probiotic strains are *Lactobacillus* and *Bifidobacterium*. Adding *Lactobacillus* to fermented milk led to a fourfold decrease in insulin growth factor -1 (IGF-1) compared with non-fermented skim milk, and theoretically, this could improve acne by decreasing IGF-1 levels.[9]

Mechanisms of action of cosmeceuticals in acne management

Cosmeceuticals can target various aspects of acne pathogenesis, and some have multiple mechanisms of action. **Table 1** above details the five key impacts of cosmeceuticals on acne pathogenesis.[3]

Common cosmeceutical ingredients in acne management

Several key ingredients are frequently found in cosmeceutical products for acne management. Their roles and mechanisms are summarised in **Table 2**.[3]

Integration of cosmeceuticals into acne treatment protocols

Cosmeceuticals are increasingly being integrated into comprehensive acne treatment protocols due to their ability to target multiple aspects of acne pathogenesis.[10] Dermatologists and skincare professionals often recommend cosmeceuticals as part of a holistic approach to acne management, alongside traditional treatments such as topical retinoids, antibiotics, and hormonal therapy.[11]

Table 2. *Key cosmeceutical ingredients.*

Ingredient	Mechanism in acne management	Common products
Niacinamide	Anti-inflammatory Sebum regulation Skin barrier restoration	Serums Moisturisers Sunscreens
Salicylic acid	Exfoliation of pilosebaceous duct to improve comedone clearance Anti-inflammatory	Cleansers
AHAs (glycolic and lactic acid)	Exfoliation	Cleansers Serums
Zinc	Anti-inflammatory Antioxidant Antimicrobial	Moisturisers Oral supplement
Vitamin C	Antioxidant	Serums
Retinoids	Regulate skin turnover Prevent comedone formation by inhibiting sebum production Non-prescription derivatives: retinol, retinyl esters, retinaldehyde	Prescription retinoids – cream; gel
Silymarin (milk thistle extract)	Anti-inflammatory Antimicrobial Antioxidant	Serums
Bukuchiol	Sebum regulation Anti-inflammatory Antimicrobial	Serums and creams
Tea tree oil	Antimicrobial	Cleanser

AHAs, alpha-hydroxy acids.

When incorporating cosmeceuticals into an acne treatment regimen, four factors should be considered:

1. **Severity of acne:**
   For mild to moderate acne, cosmeceuticals may be sufficient as standalone treatments or combined with over-the-counter acne products. For severe acne, cosmeceuticals should be used as adjunctive therapies to enhance the efficacy of prescription treatments and improve their tolerability.

2. **Skin type and sensitivity**:
   Individuals with sensitive or reactive skin may benefit from cosmeceuticals with soothing and anti-inflammatory properties, such as niacinamide or green tea extract. It is important to choose products suitable for the individual's skin type to avoid irritation or exacerbation of acne.

3. **Combination with other treatments:**
   Cosmeceuticals can complement traditional acne treatments by addressing specific concerns such as inflammation, hyperpigmentation, and skin texture. For example, a patient using a topical retinoid may benefit from a niacinamide-containing moisturiser to reduce irritation and enhance the skin barrier.

4. **Patient compliance:** Cosmeceuticals are often perceived as more tolerable and less irritating than some traditional acne treatments, which can improve patient compliance. The pleasant textures and additional cosmetic benefits of cosmeceuticals (e.g., hydration, brightening) may encourage regular use, leading to better treatment outcomes.

Limitations and considerations

While cosmeceuticals offer promising benefits for acne management, there are several limitations and considerations to consider:

1. **Lack of regulation:**
   Unlike pharmaceuticals, cosmeceuticals are not subject to rigorous testing and regulation. The quality and concentration of active ingredients vary widely between products, which may impact their efficacy. Consumers should be cautious and

seek products from reputable brands that provide transparency about their formulations.

2. **Individual variability:**
   The effectiveness of cosmeceuticals can vary depending on individual factors such as skin type, genetics, and environmental influences. What works for one person may not work for another, making it essential to individualise treatment

3. **Potential for irritation:**
   Some cosmeceuticals, particularly those containing active ingredients like acids or retinoids, can cause irritation or dryness, especially when combined with other acne treatments. Introducing new products gradually and monitoring the skin's response is essential.

4. **Cost and accessibility:**
   Cosmeceuticals can be more expensive than standard over-the-counter acne treatments, which may limit their accessibility for some individuals. Additionally, the marketing of cosmeceuticals can sometimes overstate their benefits, leading to unrealistic expectations.

5. **Therapeutic option:**
   Consider using in certain groups such as young children, pregnant women and older women with hormonal acne, as well as aiding in post-inflammatory hyperpigmentation.

Conclusion

Cosmeceuticals play an increasingly important role in managing acne vulgaris, offering a range of benefits that complement traditional acne treatments. Their ability to target multiple aspects of acne pathogenesis, such as inflammation, sebum production, and microbial colonisation, makes them valuable adjuncts in acne treatment protocols.

While cosmeceuticals are generally effective for mild to moderate acne, their use should be carefully tailored to the individual's skin type and the severity of the condition. Dermatologists and skincare professionals should consider cosmeceuticals' potential benefits and limitations when developing personalised acne treatment plans.

As research in this field continues to evolve, new and innovative cosmeceutical ingredients will likely emerge, offering even more targeted and effective options for managing acne. However, consumers should remain informed and discerning, choosing products supported by scientific evidence aligned with their specific skincare needs. As dermatologists, we must counsel our patients in selecting appropriate and affordable skin care.

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Recent Advances in Topical Antioxidants

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OUTLINE: The field of dermatology has witnessed remarkable strides in leveraging topical antioxidants, highlighting their burgeoning role in skin care. Antioxidants play a pivotal role in quenching free radicals, thereby alleviating the oxidative stress implicated in skin ageing, inflammation, and a spectrum of dermatologic maladies. An expansive array of antioxidants tailored for topical application includes vitamin C (ascorbic acid), vitamin E (tocopherol), coenzyme Q10 (ubiquinone), and polyphenols, including resveratrol and green tea extract. These compounds are well-known for their robust free-radical-scavenging properties and protective shields against skin cells.

Antioxidants have shown promising capabilities in modulating gene expression, boosting collagen production, and reinforcing the skin barrier. Their incorporation into daily skincare routines is increasingly favoured for maintaining skin health and addressing the visible signs of ageing. Innovations in formulation technologies have significantly improved the stability and bioavailability of antioxidants, thereby ensuring enhanced skin penetration and efficacy. This review explores the roles, mechanisms, and recent breakthroughs in topical antioxidants, positioning them as pivotal components of contemporary dermatological care.

KEYWORDS: antioxidants, oxidative stress, free radicals, antiaging, acne

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Introduction

Skin conditions rank fourth globally in terms of non-fatal disease burden, as reported by the Global Burden of Disease project. As the adage goes, "forewarned is forearmed." This principle is particularly relevant in dermatology, where topical antioxidants have emerged as a powerful strategy to prevent and mitigate skin damage caused by oxidative stress. Oxidative stress, primarily induced by environmental factors, such as UV radiation and pollution, leads to the formation of free radicals that damage skin cells and accelerate the ageing process.[1]

The role of antioxidants in skincare has evolved significantly, driven by innovations in their formulation and delivery, which have enhanced their efficacy and expanded their therapeutic applications. Revolutions in the formulation and delivery of antioxidants have unlocked novel uses in preventative and therapeutic dermatology.[2]

As we explore recent advances in topical antioxidants, it is evident that their integration into skincare regimens is crucial. The synergy among novel antioxidant compounds, improved delivery systems, and combination therapies marks a novel era in dermatological care dedicated to maintaining and enhancing skin health. Consequently, this review aimed to comprehensively examine the mechanisms, clinical applications, and recent advancements in topical antioxidants in dermatology, highlighting their therapeutic benefits and integration into skincare practices.

Search strategy

To comprehensively explore the role of topical antioxidants, a systematic search strategy was implemented across various academic databases, including PubMed, Web of Science, and Scopus. The search focused on keywords such as "topical antioxidants," "dermatology," "skin ageing," "oxidative stress," "free radicals," "antioxidant formulations," and "skin health." Expert opinions from dermatologists and skincare researchers have also been incorporated into industry publications, complementing academic

literature with insights into emerging trends and practical applications in dermatological practice.

Antioxidants[3]

An antioxidant may be defined as any substance that can delay or prevent the oxidation of a substrate when present in small amounts relative to the amount of the substrate. Antioxidants can act through five mechanisms: (i) lowering localised oxygen concentrations, (ii) scavenging initiating radicals to prevent chain initiation, (iii) binding metal ions to inhibit radical formation, (iv) decomposing peroxides to prevent their conversion into radicals, and (v) breaking chains to stop ongoing hydrogen abstraction by the active species.

Battling the skin's silent enemy: Oxidative stress[3]

Oxidative stress, a covert yet potent adversary, significantly affects skin integrity by disrupting the delicate balance between free radicals and antioxidants. This imbalance, exacerbated by environmental aggressors such as UV radiation and pollution and lifestyle factors such as smoking, accelerates cellular degeneration, leading to premature ageing, hyperpigmentation, acne, and a heightened risk of skin cancer. Harnessing topical antioxidants' effects, a strategic skincare regimen and dietary adjustments can effectively counteract oxidative damage. Antioxidants mitigate cellular deterioration by neutralising free radicals, preserving skin vitality and fostering robust and resilient complexes. The balance between pro-oxidants and antioxidants is crucial in maintaining skin health.

Radiant revival: Comprehensive roles of topical antioxidants in skincare antiageing[3]

Topical antioxidants are pivotal in anti-ageing skincare, protecting against oxidative stress and skin damage. They neutralise free radicals, stabilise cellular components, and prevent premature ageing. They also curb inflammation, preserve collagen and elastin, protect against UV damage, and protect against photoaging. Additionally, antioxidants enhance skin hydration and barrier function, inhibit melanin production for an even skin tone, and support DNA repair, ensuring resilient and youthful skin.

Wound healing[3]

Oxygen is essential for wound healing and aids in oxidative bacterial killing, collagen synthesis, angiogenesis, and epithelialisation. During the inflammatory phase, neutrophils and macrophages release large amounts of reactive oxygen species (ROS) to kill pathogens; however, excessive ROS damages the surrounding tissues and plays a role in angiogenesis and re-epithelialisation, with moderate levels promoting healing.

Anti-inflammation[3]

Antioxidants play crucial roles in mitigating inflammation through various mechanisms. It includes scavenging ROS, inhibiting the production and release of pro-inflammatory cytokines, thereby modulating the immune response and reducing tissue damage; the NF-κB signalling pathway is modulated by inhibiting its activation and reducing the expression of inflammation-related genes. Moreover, antioxidants stabilise cell membranes by preventing lipid peroxidation, regulating enzymes such as cyclooxygenase and lipoxygenase, decreasing the production of pro-inflammatory molecules such as prostaglandins and leukotrienes, facilitating cellular repair mechanisms, and promoting the healing of tissues damaged by inflammation.

Anti-cancer[3]

Exposure to ultraviolet radiation (UVR) leads to the formation of ROS in skin cells, potentially contributing to cutaneous malignancies. Manganese superoxide dismutase is a crucial component of antioxidant defence, and its adaptive response to repeated UVR exposure enhances mRNA levels and activity in fibroblasts. However, individual reactions to UVR vary; not all antioxidants react uniformly to UVR exposure.

Psoriasis[3]

Patients with active psoriasis exhibit consistent systemic signs of oxidative stress, characterised by elevated plasma levels of malondialdehyde, indicating the depletion of natural antioxidant systems. This leads to increased peroxidation of cell membranes and plasma lipid processes in the circulating cells. Additionally, erythrocyte levels of superoxide dismutase are reduced in patients with psoriasis. Antioxidant therapies aim to restore redox balance, potentially exerting anti-inflammatory effects by activating antiproliferative and pro-apoptotic pathways.

Acne treatment[3]

Topical antioxidants play beneficial roles in the treatment of acne via several mechanisms. Antioxidants possess anti-inflammatory properties, helping reduce inflammation associated with acne lesions

by neutralising ROS and modulating inflammatory pathways in the skin. Second, acne-prone skin often experiences increased oxidative stress, exacerbating inflammation and contributing to acne severity. Antioxidants scavenge free radicals and prevent oxidative damage to skin cells, thereby reducing oxidative stress. Third, excessive sebum production and lipid peroxidation within sebum are the main factors in the development of acne. Antioxidants avert this lipid peroxidation to alleviate the disease process. Antioxidants also support skin repair processes and collagen production, which is crucial for healing acne lesions and reducing post-inflammatory hyperpigmentation or scars.

Anti-hyperpigmentation[4]

Topical antioxidants interfere with melanogenesis and the production of melanin pigments in the skin, resulting in skin lightening. Several antioxidants scavenge free radicals and inhibit oxidative stress, inhibiting melanin production. Certain antioxidants directly inhibit tyrosinase, a crucial enzyme in melanin synthesis. This inhibition curtails the conversion of tyrosine into melanin intermediates, effectively decreasing melanin production, contributing to lighter skin tone and reduced hyperpigmentation. Finally, some antioxidants improve the skin barrier function, help prevent pigmentation issues, and promote skin tone.

Recent advances in topical antioxidants

An extensive overview of various topical antioxidants, detailing their sources, dosage forms, mechanisms of action, clinical applications, potential side effects, and recent advancements or innovations, is presented in **Table 1**. The compounds included bakuchiol, copper, curcumin, ferulic acid, genistein, glutathione, astaxanthin, carotenoids, coenzyme Q10, niacinamide, resveratrol, selenium, silymarin, zinc, vitamins A, E, and C, THDA, Epilobium angustifolium, epicatechin, and ectoin. Each entry provides specific insights into how these antioxidants function at the cellular level, their therapeutic benefits, and advancements that have enhanced their effectiveness or application in dermatological treatments.

AA, ascorbic acid; ACE, angiotensin-converting agent; AXT, Astaxanthin; BGM, bakuchiol, Ginkgo biloba extract, and mannitol; COL IV, collagen type IV; COL VI, collagen type VI; CuO NPs, copper oxide nanoparticles; ERK, extracellular signal-regulated kinase; GSH-Px, glutathione peroxidase; GSNO, S-nitroglutathione; IL, interleukin; MDA, malondialdehyde; MMP-6, matrix metalloproteinase 6; NFκB, nuclear factor kappa B; PL, pityriasis lichenoides; PUVA, psoralen plus ultraviolet-A radiation; ROS, reactive oxygen species; SOD, superoxide dismutase; STAT3, Signal Transducer and Activator of Transcription 3; THDA, tetrahexydecyl ascorbate; TNF-α, tumour necrosis factor alpha; UV, ultraviolet; UVB, ultraviolet B.

Delivery system of topical antioxidants[19]

The inherently impermeable nature of skin poses a formidable barrier to effective cutaneous drug delivery. Conventional drug dosage forms frequently fail to achieve adequate therapeutic effects owing to limited skin penetration. Gels, including hydrogels and oleogels, are the most prevalent form of topical drug administration. Advancements in drug delivery systems have led to the development of more sophisticated methods for enhancing drug efficacy and patient compliance.

Among these advanced delivery systems, lipids and polymeric nanoparticles stand out for their ability to encapsulate active ingredients and facilitate their controlled release. Microparticles, another promising vehicle, offer the advantage of sustained drug delivery over an extended period. Transferosomes, which are ultraflexible vesicles, can traverse the stratum corneum more effectively than conventional liposomes and deliver therapeutic agents deeper into skin layers.

Vesicular systems, particularly liposomes, provide versatile platforms for encapsulating hydrophilic and hydrophobic drugs, enhancing their stability and bioavailability. Liposomal encapsulation, which involves spherical vesicles comprising phospholipid bilayers, enhances the stability of antioxidants, including vitamins C and E, improves skin penetration, and allows for controlled release.

Emulsion-based systems, including microemulsions and nanoemulsions, improve drug solubilisation and penetration through the skin barrier owing to their fine droplet size and large surface area. Solid lipid nanoparticles and nanostructured lipid carriers enhance the stability and delivery of antioxidants, improve skin penetration, and allow controlled release of vitamin A and Coenzyme Q10.

Particulate systems, including microparticles and nanoparticles, have been extensively studied for their potential to improve drug delivery. These systems offer the benefits of targeted delivery, reduced dosing frequencies, and minimal side effects. Nanotechnology, which utilises nanoparticles, increases bioavailability and ensures targeted delivery to specific skin layers, effectively protecting antioxidants, such as resveratrol and Coenzyme Q10, from environmental degradation.

Table 1. *Comprehensive overview of various topical antioxidants.*

Compounds	Dosage	Mechanism of action	Clinical application	Adverse events	Advances and innovations
Bakuchiol[5] Meroterpene phenol derivative from the seeds of L. Psoralea corylifolia, Psoralea glandulosa, and Psoraleae Fructus	0.5–1.5% (w/w)	Stimulates collagen synthesis in fibroblasts and reduces IL-8 and p16 expression in ageing skin.	Anti-ageing	Redness and peeling in sensitive skin.	Rising popularity as a natural alternative to retinoids
	0.5% (w/w)	Inhibit melanin synthesis through the suppression of tyrosinase and alpha-melanocyte activity.	Anti-hyperpigmentation		
	0.1% (BGM)	Regulates seborrhoea and exhibits antibacterial properties.	Anti-acne		
	77.02%	Inhibits melanogenesis by blocking melanin synthesis and the formation of primary cilia and dendrites, involving Rho-dependent signalling and tyrosinase expression regulation.	Anti-melanogenesis		
	39 μM, 10 mM	Prevents lipid peroxidation, reduces ROS-induced apoptosis and retinal ganglion cell death, reduces Oxidative stress, and activates the S1RT1/Nrf2 pathway.	Antioxidant		
Copper[6] Trace element	PL, GSNO, and CuO NPs	Reduce cell viability and increase ROS selectively in melanoma cells rather than healthy cells.	Skin cancer	Peptide allergy rarely reported and can give mild to severe rash	Chitosan-coated copper oxide nanocomposite gel
Curcumin[7] Natural Lipophilic polyphenol from turmeric	200 mg/cm^2 twice daily	Enhance skin barrier integrity and reduce shedding of epithelial loss.	Radiation-induced skin damage	No adverse effects reported	Chitosan-alginate sponges, polymeric bandages, alginate foams, collagen films, nano-emulsion, hydrogel, and β-cyclodextrin-curcumin nanoparticle complex
Ferulic acid[8] Phenolic acid present in various plants	15% L-ascorbic acid, 1% α-tocopherol, and 0.5% ferulic acid	Free radical scavenging, by forming stable phenoxyl radicals in the reaction of the radical molecule with the antioxidant molecule, thereby inhibiting the free radical generation.	Antioxidant—reduces facial hyperpigmentation	Irritation of sensitive skin and mild skin peeling	Chitosan contained vitamin preparation B1 and vitamin B6
	14% ferulic acid	Antioxidative and anti-inflammatory activity could prevent and reduce photo-oxidative skin damage.	Anti-ageing, moisturising effects, reduced melanin and erythema and enhanced skin elasticity		

BGM, bakuchiol, Ginkgo biloba extract, and mannitol; CuO NPs, copper oxide nanoparticles; GSNO, nitric oxide donor S-nitrosoglutathione; IL, interleukin; PL, pluronic F-127; ROS, reactive oxygen species; S1RT1/Nrf2, sirtuin1/nuclear factor erythroid 2-related factor 2.

Compounds	Dosage	Mechanism of action	Clinical application	Adverse events	Advances and innovations
Genistein[9] Heterocyclic lipophilic diphenol	10, 20, and 40 μM	Inhibit the phosphorylation of ERK and STAT3, thereby downregulating the expression of inflammatory factors and chemokines.	Anti-inflammation, anti-photoaging, skin cancer, alleviate skin dryness and diminish wrinkles	Rare but genotoxic in experimental animal study	Nanotechnology-based delivery of genistein
	5 μM/cm2 was applied 30 min before exposure to UVB	Antiproliferative activity by inhibiting NFκB signalling, suppresses ACE activity and inhibits elastase release.	PUVA-induced skin thickening, as well as cutaneous ulceration and erythema		
	Genistein, vitamin E, vitamin B3, and ceramide	Prevents cytokines & TNF-α-induced NF-κB nuclear translocation, with no effect on the PI3K signalling cascade leading to attenuation of TNF-α and LPS-induced inflammatory responses by suppressing ROS activation.	Antiageing in postmenopausal women's facial skin		
Glutathione[10] Tirpeptide composed of cysteine, glutamate and glycine	N/S	Protecting cells from oxidative stress and damage by facilitating detoxification processes, including the detoxification of drugs and hydrogen peroxide.	Antioxidant	Rash and inhaled glutathione can aggravate asthma	Glutathione encapsulated liposome
	2.0% oxidized glutathione	Repair oxidative damage to protein thiols, regulating redox signalling, influencing cell proliferation, modulating the cell cycle and apoptosis, supporting the immune response, and contributing to skin pigmentation.	Skin protectant		
	2% with Vit C + SPF35 Broad spectrum sunscreen	Melanogenesis inhibition activity is thought to occur through tyrosinase inhibition, both directly by chelating copper ions on the active site of tyrosinase and indirectly through the antioxidative property described above and by shifting eumelanin (the darker pigment) to pheomelanin (the lighter pigment) production.	Skin whitening		
Astaxanthin[11] xanthophyll carotenoid naturally produced by various bacteria, microalgae, and yeasts, with the microalga Haematococcus pluvialis	78.9 μM solution	Ability to suppress oxidative polymerisation in melanocytes and reduce inflammation in the epidermis.	Anti-ageing (wrinkles, age spots, elasticity and skin texture)	Increased skin pigmentation, altered hormone levels, and hair growth.	AXT-loaded stealth lipid nanoparticles AXT non-aqueous nanoemulsion

AXT, astaxanthin; ERK, extracellular signal-regulated kinase; LPS, lipopolysaccharide; NF-κB, nuclear factor-kappa B; PI3K, phosphoinositide 3-kinase; SPF, sun protection factor; TNF-α, tumour necrosis factor alpha.

Compounds	Dosage	Mechanism of action	Clinical application	Adverse events	Advances and innovations
Carotenoids[12] fat-soluble terpene compounds synthesised by certain bacteria, fungi (yeast), algae, corals, and higher photosynthetic organisms in the presence of visible light and oxygen. Source: from fruits and vegetables	0.29–0.38 mg dry extract/mL	Scavenging free radicals	Antioxidant, mitigate inflammation thereby reducing tissue damage and promote faster healing	Skin discoloration (yellowing that eventually goes away) and bruising	Carotenoid encapsulation in lipid nanoparticle
	Mixture of tomato and rosemary extract/ 40g of tomato paste	Prevent pro-inflammatory cytokine increase	Reduce erythema		
Coenzyme Q10[13] Lipid soluble naturally present in the body Enhances other antioxidants like α-tocopherol (vitamin E) and ascorbate (vitamin C)	40% CoQ10	Scavenge free radicals, thereby reducing oxidative stress	Oral lichen planus	Allergic skin rashes	Coenzyme Q10 loaded microemulsion
	1% CoQ10 cream twice daily	Proniosomes and nanostructured lipid carriers enhance CoQ10 penetration compared to when delivered in its free form.	Anti-ageing		
Niacinamide[14] Amide form of vitamin B3 and water soluble	4% cream niacinamide	Downregulating the transfer of melanosomes from melanocytes to keratinocytes, thereby decreasing the accumulation of melanin	Melasma	Flushing of the face, especially in sensitive areas such as the cheeks and nose, and around the eyes, including redness, itching, stinging or burning	Hybrid nanogel technology
	5% Niacinamide and 2.5% benzoyl peroxide	Inhibits nuclear poly (ADP-ribose) polymerase-1 (PARP-1), expression of MHC-II and production of TNF-α, IL-1, IL-6, IL-8, and nitric oxide, leucocyte chemotaxis, lysosomal enzyme release, lymphocyte transformation, and IL-8 production through NFκB and mitogen-activated protein kinase pathways	Mild to moderate acne vulgaris		
	4% Nicotinamide	Inhibiting inflammatory cytokines through control of the NFκB-mediated transcription of signalling molecules	Discoid lupus erythematosus		

IL, interleukin; NF-κB, nuclear factor-kappa B.

Compounds	Dosage	Mechanism of action	Clinical application	Adverse events	Advances and innovations
Silymarin[15] From milk thistle plant, a polyphenolic antioxidant	0.7% and 1.4%	Scavenge free radicals and modulates enzymes involved in cellular damage and inhibit lipid peroxidation	Melasma		Silymarin pluronic-lecithin organogel
	0.5% serum		Acne vulgaris		
	Hexylresorcinol, silymarin, 20% vitamin C, and 5% vitamin E		Protects skin against UV radiation Skin brightening		
Vitamin C[16]	0.75% to 20%	Inhibit melanin synthesis, through downregulating monophenolase activity of tyrosinase enzyme	Melasma	Hypopigmentation, rebound hyperpigmentation, and ochronosis	Vitamin C squalene biconjugate
	0.5% retinol treatment combined with a moisturiser with 30% vitamin C	Regulating collagen production, stimulating type I procollagen synthesis in skin fibroblasts, and promoting the stability of collagen molecules	Hyperpigmentation, wrinkles, and overall photodamage		
THDA[17] Lipid-soluble derivative of vitamin C, known as a pro-vitamin C	10% (vitamin C) and 7% THDA	Enzymatic conversion to vitamin C within the dermis increases COL IV and COL VI proteins	Photodamaged skin	Burning, crusting, dryness, flaking, itching, oozing, pain, redness, sores or ulcers, or swelling.	Liposome encapsulated THDA and restored with IL-6, IL-8, and MMP-6 levels
Ectoin[18] Cyclic amino acid, naturally synthesised by extremophile microorganisms shield cells from chemical and physical stressors—protects cell membranes from dehydration-induced reactions and subsequent inflammation by forming a water shell (ectoine hydrocomplex) around proteins.	2% ectoin	Decrease intracellular levels of ROS and MDA while increasing the activities of SOD and GSH-Px	UVA-induced and H_2O_2-induced oxidative damage	Burning sensation, tingly sensation, reddening, and exacerbation of skin	Liposome encapsulated ectoin

COL, collagen; GSH-Px, glutathione-peroxidase; MDA, malondialdehyde; MMP-6, matrix metalloproteinase 6; ROS, reactive oxidative species; SOD, superoxide dismutase; THDA, tetrahexyldecyl ascorbate; UV, ultraviolet; UVA, ultraviolet A.

Inclusion complexes, which involve the encapsulation of active molecules within larger molecules, enhance the solubility and stability of drugs and facilitate their penetration into the skin. Microencapsulation stabilises sensitive antioxidants, including astaxanthin and curcumin, controls their release rate, and reduces skin irritation. Hydrogels and hydrocolloids, which are water-based gels, provide sustained release, enhance hydration, and increase skin contact time, making them ideal for delivering vitamin C, vitamin E, and polyphenols as moisturising and anti-ageing products.

Films, another innovative approach, provide a controlled release matrix that can be applied directly to the skin, ensuring prolonged contact and sustained drug delivery. These advanced carriers can subsequently be formulated into creams and gels, making them more user-friendly and improving patient adherence to treatment regimens.

Microneedle patches, equipped with tiny needles that create microchannels in the skin, enhance skin penetration and increase the efficacy of antioxidants, including vitamin C and niacinamide. Prodrug formulations chemically modify antioxidants to enhance their stability and skin absorption, converting them into their active forms once absorbed. This approach is particularly effective for retinoids and vitamin C derivatives, improving their effectiveness and reducing irritation. These innovations are pivotal for maximising the benefits of topical antioxidants and ensuring that they reach the desired skin layer, remain stable, and provide sustained therapeutic effects.

Recent studies regarding various antioxidants

An extensive overview of the different antioxidants, detailing their study design, population, ingredients, and study findings, is listed in **Table 2**.

Table 2. *Various studies on topical antioxidants.*

Author	Study Design	Ingredients	Study Findings
Rao S, Goldberg D (2023)[20]	Open-label clinical trial	0.2% pure retinol, 2.5% tripeptide concentrate, and 5.0% glaucine complex (Tripeptide-R Neck Repair, Skinceuticals)	A new topical cream effectively improved signs of photoaging by increasing dermal collagen and GAGs.
Sullivan et al. (2023)[21]	Clinical trial	Retinol, tripeptide complex, and glaucine	The topical product effectively treated the ageing signs on the neck skin. There was a significant improvement in a myriad of neck ageing attributes, including fine lines/wrinkles, crepiness, laxity, and texture.
Draelos Z D et al. (2024)[22]	Single centre, Clinical study	0.5% silymarin, 15% L-ascorbic Acid, 0.5% ferulic acid	Silymarin antioxidant serum significantly improved skin clarity, PIH, skin tone evenness, and overall appearance, fulfilling anti-ageing and acne needs.
Ferrara F et al. (2024)[23]	Single-blinded, clinical study	15% ascorbic acid, 0.5% ferulic acid, and 1% tocopherol (CF Mix)	CF Mix demonstrated a protective effect against the damage exerted by PM + UV for all the markers tested, suggesting its promising protective role against damaging events induced by prolonged exposure to pollutants.
Ferrara F et al. (2024)[24]	Descriptive study	15% vitamin C (L-ascorbic acid), 1% vitamin E (α-tocopherol), and 0.5% ferulic acid	Daily topical of an antioxidant application may prevent pollution-induced skin damage.

GAG, glycosaminoglycan; PIH, post-inflammatory hyperpigmentation; PM, particulate matter; UV, ultraviolet.

Latest delivery systems in cosmetic dermatology [25–27]

The cosmetics industry uses cutting-edge delivery systems to encapsulate natural ingredients effectively. Cubosomes, liquid-crystalline particles formed by the self-assembly of amphiphilic molecules, are nanostructured. They provide biocompatibility, thermodynamic stability, and controlled release capabilities. The bottom-up manufacturing approach for cubosomes is favoured for large-scale production owing to its lower energy requirements and enhanced stability.

Dendrimers, highly branched polymer-based systems, offer adjustable loading capacity, controlled physicochemical properties, and manageable viscosity, making them ideal for cosmetic formulations. They are synthesised via divergent or convergent assembly, with the convergent approach providing precise control over their molecular weight and functionalities.

Nanocrystals enhance solubility and dissolution rates of poorly soluble active ingredients. Composed mostly of active ingredients with stabilisers, they are incorporated into formulations via an aqueous nanocrystal concentrate. The top-down approach is more industrially relevant despite challenges such as long operation times and high energy consumption.

The continued positive response of antioxidant formulation on extracellular matrix following laser-assisted delivery is an exciting chapter in modern dermatology. Antioxidants like vitamins C and E, and ferulic acid correspond by reciprocating accelerated wound healing post-fractional ablative laser. A recent study highlighting the combination of antioxidants delivered by micro-needle mesotherapy and sonophoresis also demonstrated enhanced anti-ageing effects.

Continued research is essential to advance these systems. The focus areas include enhancing the cubosome loading capacity and controlled release, developing methods for medium-solubility active ingredients in nanocrystals, and integrating these delivery systems to uncover new applications and insights.

Conclusion

Integrating topical antioxidants into dermatological practice represents a significant advancement in skincare, driven by recent scientific and clinical innovations. Advancements in formulation technologies have overcome the previous challenges related to stability and bioavailability, making these compounds more effective in clinical and consumer products. The diverse clinical applications of antioxidants, ranging from anti-ageing to acne management, underscore their versatility and importance in dermatological treatment. Recent advancements support the development of targeted therapies and personalised skincare regimens, ultimately enhancing patient care and outcomes in dermatology.

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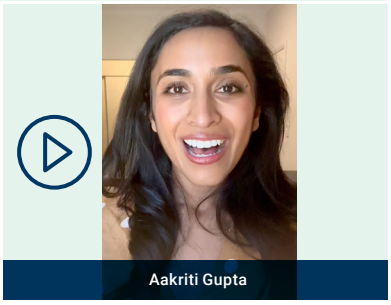
Is There an Ideal Skin Routine? A Comprehensive Review



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OUTLINE: The rapid expansion of the skincare industry, fuelled by the rise of social media "skinfluencers," has significantly increased public interest in identifying an "ideal skincare routine." This growing demand has placed dermatologists at the forefront of navigating an increasingly complex array of skincare products and regimens.

This article provides a comprehensive review of critical elements in modern skincare. Key topics include the timing and layering of products to maximise efficacy, the role of ancillary skincare products such as exfoliants and masks, and a critical analysis of common myths surrounding skincare. The aim is to offer dermatologists a practical and evidence-based framework to help patients make informed choices in an environment often saturated with misinformation.

KEYWORDS: skincare, antiaging, cosmeceuticals, botanicals, sunscreen

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Introduction

The growth of the skincare industry, coupled with the impact of social media 'skinfluencers,' has increased public interest in an 'ideal skincare routine'. As a result, dermatologists are increasingly called upon to navigate product selection and the formulation of personalised skincare routines. This article seeks to provide a comprehensive overview of key aspects of skincare, including evidence-based recommendations on the timing and layering of products, the role of ancillary skincare items, and an analysis of common misconceptions. This aims to assist dermatologists in guiding patients toward effective skincare practices in a landscape of conflicting information.

The right order: Enhancing skincare efficacy through proper application

Layering

Given the increasing complexity of skincare routines, it is important to understand how to layer skincare products (**Table 1**).

Table 1. *Recommended order of skincare.*

1. Cleanse
2. Active serum (if using)
3. Eye cream (optional)
4. Moisturiser
5. Sunscreen (in the morning)

Products with high acid levels, especially if the pH is <4, can react with retinol and niacinamide, making them less effective. This may include products that contain L-ascorbic acid, alpha-hydroxy acids (AHAs) such as lactic and glycolic acid), or beta-hydroxy acids like salicylic acid.[1]

It is important to note that these interactions are related to pH rather than a class effect. For example, niacinamide can be combined with ascorbyl glucoside (a precursor to L-ascorbic acid) but not directly with L-ascorbic acid.

Certain skincare ingredients are best used either in the morning or evening.

Morning

Vitamin C-containing products are best used in the morning. This is because Vitamin C is a potent antioxidant and functions to protect our skin cells from damage by free radicals that are generated by environmental factors, including ultraviolet (UV) radiation and pollution.[1,2]

Sunscreens should be the final step in the morning skincare routine. Organic (chemical) or mineral (physical) sunscreen can be used. In Australia especially, it is best to look for a broad-spectrum sunscreen that protects against UVA and UVB, preferably with a sun protection factor (SPF) of 50+. If there are pigmentary concerns such as melasma, a physical sunscreen is generally preferred as it protects against visible light.

Evening

Vitamin A-based products, such as retinols or prescription topical retinoids, are recommended for use at night. This is because retinols and retinoids make our skin more sensitive to UV and undergo photodegradation in the presence of sunlight, making them less effective.

This also enables overnight regeneration as vitamin A regulates new cell production and stimulates collagen production.

Vitamin B3 (niacinamide) is often used in the evenings and can be safely layered with most forms of vitamin A. These two vitamins work synergistically to improve uneven skin tone and reduce fine lines.[1] As it is photostable, vitamin B3 can be used in the morning and/or evening depending on the other cosmeceuticals being used.

The role of ancillary skincare products

Exfoliants

Exfoliants are typically used once or twice per week and can be physical or chemical in nature.

Physical exfoliants

Physical exfoliants or 'scrubs' are manually massaged into the skin and work by dislodging corneocytes. This improves the skin's visual and tactile 'smoothness'. This also increases light reflection from the skin's surface, perceived as improved radiance and luminosity.[3]

Physical exfoliants often contain aluminium oxide, coffee grounds, walnut husks, ground fruit pits and/or polyethylene beads. The latter has fallen out of favour and is banned in certain areas due to environmental concerns.[4]

More frequent and/or aggressive use of exfoliants can damage the skin's barrier function, increasing skin sensitivity and promoting milia formation.

Physical exfoliants

AHAs are commonly used to provide anti-ageing benefits by stimulating exfoliation and skin renewal. AHAs are known as 'fruit' acids as they naturally occur in fruits and foods. These agents remove dead surface skin cells of the stratum corneum and stimulate the production of glycosaminoglycans and collagen.

Glycolic acid and lactic acid are common AHAs that are also used in superficial peels. Salicylic acid is a beta-hydroxy acid that helps target acne-prone skin but can result in dermal thinning, in contrast to AHAs, which increase dermal biosynthesis.[5]

Newer generation AHAs include polyhydroxy acids (PHAs) such as gluconolactone and bionic acids (bionics) such as lactobionic acid. These have similar skin-smoothing and anti-aging properties to traditional AHAs but are more suitable for sensitive skin. In addition, these agents can improve the skin barrier and function as humectants and moisturisers. PHAs also have antioxidant properties and can scavenge free radicals from environmental factors such as UV radiation. Of note, they do not result in increased photosensitivity.[5]

Face masks

Face masks are applied to the skin for a short period of time, typically less than 30 minutes and can provide temporary benefits depending on type.

Commonly available masks include:

- **Clay** – these are used on acne-prone skin to absorb excess oil
- **Polymer** – commonly known as 'sheet masks,' they occlude the skin and temporarily boost skin moisture levels
- **Botanical** – these are comprised of dried plant ingredients mixed with water to form a paste. Primarily used for relaxation and aromatic benefits, they offer limited skin texture or tone improvement.[6]

Toners

Toners, or astringents, are intended for use either as an alternative to or following the use of a cleanser. Their formulations vary depending on skin type, with one of the most significant differences being alcohol concentration. Formulas for oily skin typically contain higher alcohol concentrations, while alcohol-free versions are formulated for dry skin. Humectants like propylene glycol and water are commonly included in

toners for dry skin to help retain moisture. Exfoliating toners often contain alpha-hydroxy acids, such as glycolic acid.

When an effective cleanser is used, toners are often considered an optional step in a skincare routine rather than a necessity.[4]

Skincare science: Breaking down myths and misinformation

Are 'all-natural' skincare products safe?

The term 'all-natural' is primarily a marketing label rather than a meaningful indicator of safety or efficacy.[7]

It typically refers to active ingredients derived from plants and minerals. However, virtually everything we encounter originates from natural materials found on Earth.

In Australia, cosmetic products, even if described as 'natural' or 'organic', are generally regulated as industrial chemicals due to the processes used to extract naturally occurring chemicals from their source.[8] The Australian Industrial Chemicals Introduction Scheme regulates this unless the cosmetic product makes therapeutic claims, in which case it is regulated by the Therapeutic Goods Administration (TGA).

The origin of an ingredient—whether naturally sourced or synthetically produced—does not necessarily determine its safety. For example, iron oxide pigments, commonly used in cosmetics, are often synthesised because naturally occurring iron oxides can contain higher levels of toxic heavy metals.

'All natural' ingredients are not inherently safer in the realm of skincare. Moreover, the unjustified demonisation of many safe and effective skincare ingredients may inadvertently increase exposure to more harmful substances. This narrative is also frequently perpetuated by companies with a financial interest in promoting their 'natural' skincare lines. Notably, many 'natural' products contain high concentrations of botanical extracts, which are a leading cause of irritant and allergic contact dermatitis.[6]

Do cosmeceuticals improve signs of facial ageing, and can moisturisers reduce wrinkles?

Cosmeceuticals can improve the appearance of facial ageing. However, it is important to note that claims about their efficacy are classified as cosmetic rather than pharmaceutical.[9] In Australia, the TGA does not evaluate cosmetics unless they make *therapeutic* claims. This why cosmeceuticals often claim to 'visibly correct dark spots' rather than fade pigmentation or 'target acne-prone skin' rather than improve acne.

Moisturisers can reduce the *appearance* of wrinkles by increasing skin hydration. They contain occlusive agents (e.g., petrolatum, mineral oil, or dimethicone) that reduce transepidermal water loss, thereby increasing the skin's water content and turgor. This improves the appearance of wrinkles resulting from compromised barrier function of the stratum corneum.

Some moisturisers have 'wrinkle blurring' properties. These usually include silicone gels that fill in wrinkle crevices, along with small light-reflective particles that can help reduce the visible depth of wrinkles. Whilst this can lead to a significant improvement in the appearance of wrinkles, this is based on an optical effect and lasts only as long as the product remains on the skin.[9]

Are expensive moisturisers better?

In many cases, the most expensive components of a moisturiser are its fragrance and packaging. At its core, a good moisturiser primarily requires an occlusive agent, a humectant, and a silicone-based ingredient.[9]

That said, modern moisturiser formulations are becoming more advanced, incorporating ingredients that offer benefits beyond simple hydration. For example, these may include niacinamide and panthenol (vitamin B5) for their soothing and anti-inflammatory effects, or tocopherol (vitamin E) for its antioxidant properties.

Using unique or rare ingredients believed to provide additional skin benefits can also contribute to expense. These have included saffron, liquorice root extract, gold, and diamond powder! However, assessing the true effectiveness of these ingredients is challenging without double-blind, vehicle-controlled studies, which are lacking in the current literature.

For example, a high-end skincare line, where moisturisers start at $500, features rare caviar sourced from the endangered beluga sturgeon. The high cost is partly due to the rarity of the sturgeon, as the caviar must be harvested fresh during the natural spawning process and immediately transported to the lab for processing.[9]

Are dietary antioxidants more effective than topical vitamins?

The evidence regarding dietary antioxidants and skin ageing has been mixed. Oxidative stress, a key factor in skin ageing, occurs due to the imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defences. While the role of dietary antioxidants in cardiovascular and neurological health is well established, their impact on skin health is still being researched.

Certain effects of topical vitamins cannot be replicated through oral intake. For example, topical vitamin E acts as an emollient, improving skin texture and smoothness, whereas orally, vitamin E functions as an antioxidant but does not tend to enhance skin hydration. This demonstrates that different forms of vitamins—topical or oral—can offer distinct benefits.

What about "Botox in a bottle"?

These cosmeceuticals contain peptides that aim to relax facial muscles by targeting the neuromuscular junction. Argireline is the most commonly used neurotransmitter peptide, and it is thought to disrupt the release of acetylcholine at the neuromuscular junction by destabilising the protein complex involved.

For a neuromuscular peptide to work, the formulation must achieve three key things:

1. It must penetrate deep enough to reach the neuromuscular junction.

2. It must reach a sufficient concentration to create a visible difference.

3. It must remain in place long enough to produce a sustained effect.

Achieving these outcomes with a topical formulation is challenging, and ongoing research and clinical trials are needed to verify its efficacy.[9] It is also important that these studies isolate the specific effect of the peptides. For example, a clinical study in Germany that isolated the effect of argireline from other ingredients in a cosmeceutical formulation that can reduce the appearance of wrinkles, such as hyaluronic acid, found no statistically significant difference in split-face comparisons.[10]

Do sunscreens with SPF > 15 offer significantly greater sun protection?

SPF is not an absolute protection rating but rather a relative measure of a sunscreen's ability to prevent sunburn. For instance, correct use of an SPF 15 sunscreen allows an individual to stay in the sun 15 times longer before experiencing sunburn than if they were not using the sunscreen. SPF is a measure of UVB protection. As the SPF further increases, the 'per cent increase' in UVB protection is less marked, as seen in **Table 2**.[1,11]

Table 2. *UVB photoprotection provided by a given SPF.*

SPF	% UVB Radiation Blocked
4	75
15	93
30	97
50	98

Looking at the table, an SPF 4 sunscreen blocks 75% of UVB radiation, while an SPF 15 blocks 93%, which is a significant difference. However, doubling to SPF 30 only increases UVB protection by an additional 4%.

We recommend using higher SPFs because real-world applications are often less than those tested in clinical trials. Sunscreen may be applied unevenly or migrate over the skin surface throughout the day, resulting in an incomplete sunscreen film over the skin surface. As a result, the sunscreen may not deliver the labelled SPF amount of sun protection. Frequent reapplication is also essential to ensure adequate protection.

Broad spectrum sunscreens protect against both UVB and UVA radiation; to achieve this, sunscreens need to have an SPF of at least 30.[9]

What are the controversies surrounding 'nanoparticles' and the use of zinc oxide (ZnO) and titanium dioxide (TiO_2)?

There are two main concerns relating to the use of nanoparticles. Firstly, ROS may form metal oxide nanoparticles on exposure to UV and these may be cytotoxic and carcinogenic.

The second concern relates to whether these nanoparticles can penetrate the epidermis and reach the human blood stream and potentially cause toxicity with long-term use. Both *in vivo* and *in vitro* studies to date have shown that the nanoparticles remain confined to the non-viable keratinised layer of the epidermis, the stratum corneum, after topical application even in situations where skin barrier function has been disrupted.[11,12]

Furthermore, manufacturers now coat nanoparticles with compounds like aluminium oxide to reduce the formation of ROS and prevent nanoparticles from adhering to cells.[11]

The TGA's *Literature review on the safety of titanium dioxide and zinc oxide nanoparticles in sunscreens* concluded that the evidence at publication did not suggest that TiO_2 and ZnO nanoparticles reach the general circulation.[13]

Conclusion

In an industry driven by the promise of beauty ideals, distinguishing scientific fact from marketing fiction is difficult. This article aims to provide dermatologists with a clearer understanding of essential skincare principles, enabling them to offer more precise, evidence-based recommendations for personalised skincare routines. By focusing on key elements such as product selection, layering, and addressing common misconceptions, the goal is to help professionals navigate the spin and help patients achieve healthier skin.

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Trends in Cosmeceutical Ingredients

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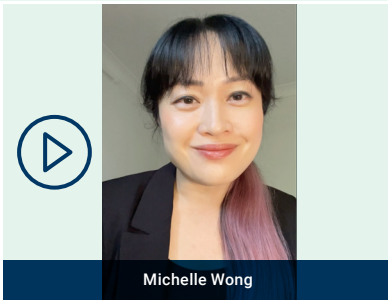

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Disclosures: Michelle Wong and Hannah English have consulted for L'Oreal and P&G.

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OUTLINE: Current cosmeceutical trends are driven by regulatory changes, consumer demand, and the need for product differentiation. Increasingly, skincare formulations are using derivatives and advanced delivery systems, and ingredients to support novel claims surrounding exosomes, microbiome, pollution, menopause, and sustainability. This article explores current trends in cosmeceutical ingredients, with a focus on mechanistic plausibility and credibility of evidence.

KEYWORDS: active ingredients, cosmeceuticals, skincare, cosmetics, pharmacology

Wong M and English H. Trends in cosmeceutical ingredients. Opin Prog Cosmet Dermatol. 2025;4(2):30–35.

Introduction

Social media has provided consumers unprecedented access to skincare ingredient information, though its accuracy is often questionable. Active ingredients and long-term benefits can be found even in budget skincare products. To remain competitive in a saturated market, brands employ more sophisticated formulation technologies and introduce novel claims extending beyond traditional cosmeceutical benefits. New regulations also drive changes in ingredient selection.

This article explores current trends in cosmeceutical ingredients, focusing on mechanistic plausibility and credibility of evidence.

Table 1. *Therapeutic Goods (Poisons Standard) classification.*[1]

Schedule 1	Not currently in use
Schedule 2	Pharmacy Medicine
Schedule 3	Pharmacist Only Medicine
Schedule 4	Prescription Only Medicine OR Prescription Animal Remedy
Schedule 5	Caution
Schedule 6	Poison
Schedule 7	Dangerous Poison
Schedule 8	Controlled Drug
Schedule 9	Prohibited Substance
Schedule 10	Substances of such danger to health as to warrant prohibition of sale, supply, and use

New permitted ingredients

The Australian Poisons Standard (**Table 1**) significantly influences the regulation of cosmetic ingredients, especially those with potential risks.[1] Recent amendments to the schedule have implications for the selection of cosmeceutical ingredients and subsequent product formulations (**Table 2**).

Table 2. *Recent changes to cosmeceutical ingredient classifications in the Australian Poisons Standard.*[1–3,6]

Ingredient	Previous scheduling	Updated scheduling
Hydroxypinacolone retinoate	Schedule 4 with warnings for pregnancy and potential birth defects	Unscheduled in preparations for dermal use containing 0.5% or less of hydroxypinacolone retinoate
Azelaic acid	Schedule 2 or Schedule 4 unless present at 1% or less	Schedule 5 with safety instructions except when included in schedules 2 or 4
Tranexamic acid	Schedule 4	Unscheduled in preparations containing 3% or less of tranexamic acid for dermal cosmetic use

As of 01 February 2023, the Therapeutic Goods Administration (TGA) reclassified hydroxypinacolone retinoate (HPR), a retinoid ester, from Schedule 4 (a prescription-only medicine) to unscheduled for dermal use at concentrations up to 0.5%.[2] Notably, HPR was previously captured under the entry for tretinoin and exemption was granted due to its limited bioconversion to tretinoin.[3] In contrast, the TGA rejected a similar reclassification for ethyl lactyl retinoate as its *in vivo* conversion rate to tretinoin could not be established.[4] All other tretinoin derivatives remain classified as Schedule 4.

Azelaic acid is a dicarboxylic acid with antimicrobial, anti-inflammatory, and antioxidative effects used to treat acne vulgaris and rosacea. Evidence also exists for the management of pigment disorders.[5] As of 01 October 2024, azelaic acid has been reclassified under Schedule 5 (caution) for cosmetic use, with first aid and safety instructions. Therapeutic products remain classified as Schedule 2 (pharmacy medicine) or 4.[6] This could increase the availability of international cosmeceuticals containing azelaic acid or stimulate domestic product development.

Although topical cosmetic products containing tranexamic acid have been available in the Australian market, before 01 October 2024, tranexamic acid was classified as a Schedule 4 substance. A recent TGA decision has permitted the inclusion of up to 3% tranexamic acid in dermal cosmetic products, reflecting its low-risk safety profile for topical application.[6] It is included in pigment-fading products, although appropriately controlled clinical evidence remains elusive, and its properties are far outside the range for stratum corneum penetration.

Derivatives

Traditional active ingredients like retinoids and vitamin C dominate the cosmeceutical market due to their established reputation amongst consumers and the substantial clinical data supporting their efficacy. However, direct use of these compounds is often limited by stability, bioavailability, or undesirable side effects. In addition, there are new restrictions on the use of some established cosmeceutical ingredients in the European Union (**Table 3**).[7]

One strategy to circumvent these limitations is using derivatives, which are chemically modified versions of the active ingredient. After absorption into the skin, derivatives are metabolised back to the parent active ingredient, much like prodrugs in pharmaceuticals. However, *in vivo* metabolism is often poorly substantiated, and many derivatives do not demonstrate their own biological activity.

Ascorbic acid (vitamin C) decomposes rapidly in aqueous skincare formulas, which is accelerated by heat, light, and oxygen exposure.[8] Derivatives of ascorbic acid use protecting groups to block reactive centres and prevent premature degradation. Many are also more lipophilic and penetrate more readily through the stratum corneum. Popular derivatives include magnesium ascorbyl phosphate, ascorbyl glucoside, and tetrahexyldecyl ascorbate (also called ascorbyl tetraisopalmitate). The acidic hydrogen of ascorbic acid is removed in most derivatives, which reduces irritation. One notable exception is 3-O-ethyl ascorbic acid, which has much greater stability than ascorbic acid but has similar irritation potential.[9]

Retinoid derivative use has expanded due to new restrictions on retinol, retinyl acetate, and retinyl palmitate. These need to be converted to retinoic acid (tretinoin) to exert classic retinoid effects, like improving fine lines and uneven pigment (**Figure 1).** Interestingly, retinal is not restricted despite its greater potency, leading to a surge in popularity. Newer retinoate ester derivatives like retinyl retinoate, hydroxypinacolone retinoate and ethyl lactyl retinoate have also found increased use, although clinical data on these is sparse. A fatty alcohol ester of adapalene (oleyl adapalenate) has also recently been launched, but clinical evidence is not yet public.[10] The availability of adapalene as a pharmacist-only (Schedule 3) ingredient may also limit its utility.

Table 3. *Updated restrictions on cosmeceutical ingredients, applicable to cosmetic products sold in the European Union from 2025.*[7]

Ingredient	Maximum concentrations in ready-for-use preparations	Other restrictions
Retinol **Retinyl acetate** **Retinyl palmitate**	0.05% retinol equivalents in body lotions 0.3% retinol equivalents in other leave-on and rinse-off products	
Kojic acid	1% in face and hand products	
Alpha arbutin	2% in face creams 0.5% in body lotions	Hydroquinone levels must be as low as possible, and below the unavoidable trace level
Arbutin	7% in face creams	Hydroquinone levels must be as low as possible, and below the unavoidable trace level
Daidzein	0.02%	
Genistein	0.007%	

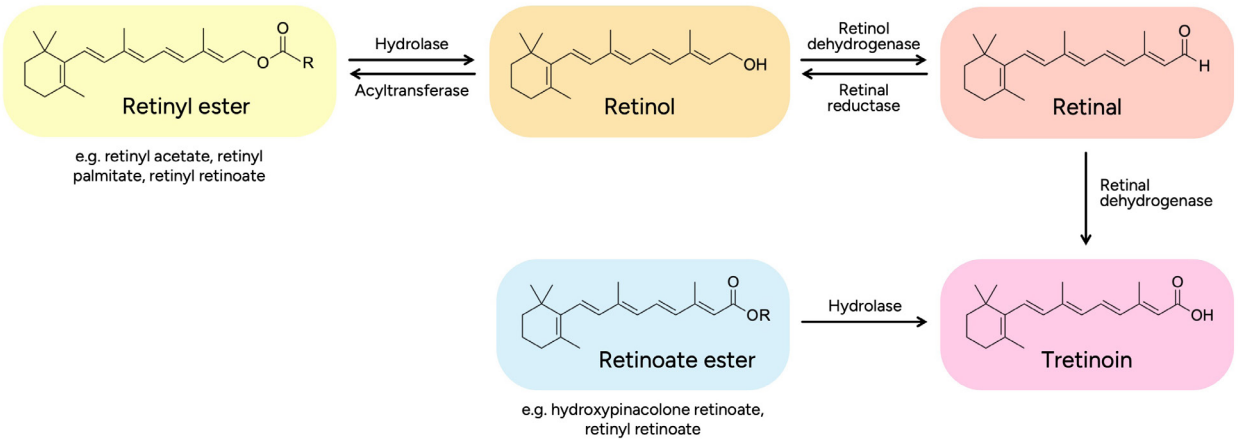

Figure 1. *Metabolism of retinoid derivatives in the skin.*

Advanced delivery systems

Initially developed for pharmaceutical applications, advanced delivery systems have found broader use in cosmetics and are increasingly found even in simple formulas. They can improve ingredient stability and skin absorption, allowing results to be achieved with lower total active concentrations. They can also allow controlled release, reducing potential irritation. However, care must be taken during formulation to ensure the active ingredient is not released before use, or retained too long in the formulation after skin application.

A trending delivery approach is encapsulation, where active ingredients are encased in a protective material. For example, liposomes are spherical nanoscale vesicles composed of phospholipids, reflecting the structure of cell membranes. While the ability of conventional liposomes to enhance delivery is limited, as they are largely confined to the stratum corneum, transdermal delivery has been reported with newer modified liposomes like transfersomes, ethosomes, and niosomes.[11] Cyclodextrins are another form of encapsulation currently used in almost all retinal formulas on the market. These macrocyclic glucose rings have relatively hydrophobic cavities, capable of forming inclusion complexes with a range of small molecules.[12]

Microneedles enhance ingredient penetration by creating microchannels in the stratum corneum and are being incorporated into novel product forms. Dissolvable microneedle patches are a popular single-use product for targeted treatment.[13] Active ingredients are embedded in the microneedles, usually made from hyaluronic acid. Upon application, the needles slowly dissolve and release their payload. Specialty packaging is necessary to protect the microneedles from moisture and physical damage. Exclusion of water also improves the stability of some active ingredients.

A new trend in Korean cosmetics is microscopic needle-like silica structures called spicules, sourced from marine sponges (INCI: hydrolysed sponge).[14] These are loaded with active ingredients and disrupt the barrier for better penetration. They also provide mechanical exfoliation as they are massaged into the skin.

Exosomes

Exosomes are extracellular vesicles derived from varying cell types and play a pivotal role in intercellular communication. Their potential to influence angiogenesis, cell proliferation, differentiation, apoptosis, and inflammation has generated significant interest in aesthetic medicine.[15] Proposed uses include scar revision, hair growth, pigmentation disorders, and skin rejuvenation.[16] While exosomes' contents and therapeutic potential vary widely depending on their origin, their applications in topical or needling cosmetic formulations are being actively investigated. However, most existing studies are preclinical, with limited clinical safety or efficacy evidence. The complexity of exosomes makes it challenging to predict their outcomes, and the U.S. Food and Drug Administration currently advises against using exosomes due to a lack of safety and efficacy data.[17] The TGA is yet to comment.

Internationally, the cosmeceutical skincare market features a variety of exosome-based products derived from diverse sources, including human platelets, human adipose-derived stem cells, and non-human sources such as rose, lavender, Centella, or Lactobacillus. Given the complexity of exosomes and the fact that awareness regarding their origins and specific benefits is still being

developed, the term "exosomes" in cosmeceuticals may be primarily a marketing buzzword until further research and education are available.

Microbiome

The skin microbiome – the community of microorganisms on the skin's surface – has been the subject of much research.[18,19] However, skin microbiome research is in its infancy, and what constitutes a "healthy" skin microbiome is not well defined, let alone which topical ingredients or products could help one achieve this. As such, claims such as "microbiome gentle" and "nourishing the microbiome" have been the subject of deceptive advertising complaints, and the effectiveness of ingredients that purport to act by impacting the microbiome should still be substantiated with reference to clinical outcomes.[20,21]

Probiotics (living beneficial microbes) cannot be incorporated in traditional topical products, which are preserved against microbial contamination. Instead, many skincare lines contain postbiotics, increasingly marketed as "probiotic extracts". These are dead microorganisms or their metabolic products, often called ferments or lysates. Their composition and effects depend on the microorganism and the fermented material. While the microbiome trend has renewed interest in postbiotic ingredients, many have been used in skincare for a long time, including ferments from Galactomyces (SK-II Pitera, Missha Time Revolution) and Bifidobacterium (Estee Lauder Advanced Night Repair, L'Oreal Youth Code, Lancôme Genifique).[22,23]

Many ingredients claim to be prebiotics, which act as a food source for beneficial microbes and encourage their growth, but these do not have many demonstrated applications outside of hydration.

Pollution

The proliferation of anti-pollution claims reflects growing consumer concerns about environmental exposure. Recent media discussions have even introduced the concept of the skin's exposome, and emerging research is elucidating the role of specific pollutants and the aryl hydrocarbon receptor (AhR) in the cutaneous effects of air pollution (**Table 4**).[24,25]

While antioxidant and film-forming ingredients are prominent in current anti-pollution cosmeceuticals, research suggests that mitigating air pollution-related skin damage is best achieved through improving indoor air quality, strengthening the skin's barrier with moisturisers, adequate but not overzealous cleansing, sun protection and antioxidants, with emerging research on postbiotic technology and even an AhR antagonist.[25–29] When evaluating anti-pollution cosmeceuticals, it is essential to consider the specific skin concerns being addressed and the evidence supporting ingredient efficacy.

Table 4. *Skin concerns associated with air pollution and causative chemical species.*[24,25]

Cutaneous effects	Relevant air pollutants
Increased trans-epidermal water loss	Particulate matter
Erythema	Polycyclic aromatic hydrocarbons
Dyspigmentation	Carbon monoxide
Inflammation	Reactive nitrogen species
Altered sebum composition and excretion	Reactive oxygen species
Stratum corneum damage	Volatile organic compounds
Disrupted skin microbiome	
Accelerated wrinkling	
Exacerbated eczema	
Increased expression of AhRs	
Worsened UV damage	

AhR, aryl hydrocarbon receptor.

Menopause

The ageing global population has caused a boom in menopause-specific products, including skincare. Menopause is associated with skin changes, including loss of collagen, thinning, dryness and sensitivity, largely due to decreased oestrogen production. While many menopause skincare products are simply rebranded anti-wrinkle formulas with added moisturising ingredients, some products specifically target hormonal pathways.

There is increased consumer interest in topical use of oestrogen due to viral social media posts recommending facial application of vaginal oestrogen creams, as well as aggressive marketing of compounded oestriol formulas by several overseas teledermatology companies. While topical application should reduce systemic effects and there is some clinical evidence for improvements in menopausal skin, the extent and risks of systemic absorption are not well characterised.[30] Hormone-sensitive conditions like melasma may also be exacerbated.

Selective targeting of oestrogen receptors may be a promising approach to reduce systemic risks further. There are two major oestrogen receptor subtypes, ERα

and ERβ. ERβ is more highly expressed in the skin and less closely associated with reproductive cancers.[30] The phytoestrogens genistein, daidzein and (S)-equol preferentially bind to ERβ and have improved signs of skin ageing in studies, but they seem to be less potent than topical oestrogens.[31]

Another promising ingredient is methyl estradiolpropanoate. This ester can act on oestrogen receptors in the skin but is rapidly metabolised to the inactive carboxylic acid when absorbed into the blood, limiting potential systemic effects. Currently, only manufacturer-funded studies are available.[32–34]

Sustainability

Sustainability is a growing consumer concern, especially amongst younger demographics. While many eco-conscious trends are largely greenwashing, increasing regulatory scrutiny requires more rigorous substantiation of any environmental claims.[35]

In response, many suppliers are offering ingredients with data to support sustainability claims, including:[36,37]

- Ingredients produced from the waste materials of other processes (upcycling), or from renewable feedstocks
- Life cycle assessments to quantify carbon and water footprints
- Traceable supply chains
- Biodegradability, usually tested with OECD 301 or 310 methods

Other trends

Clean beauty continues to dominate a substantial portion of the cosmetic market. This pseudoscientific concept relies on the idea that certain ingredients are "dirty", and their use leads to health and environmental harms. However, this conflicts with the fundamental toxicological principle that risk depends on exposure and ingredient classifications are usually based on the appeal to nature fallacy. Current trends include demonising organic sunscreens, promoting beef tallow as a panacea, and increased use of the term "non-toxic".

"Retinol alternative" has become a prominent category, consistent with the clean beauty trend. These anti-ageing ingredients claim to be more natural, less irritating, and safer to use in pregnancy than retinol. However, they have little mechanistic similarities to retinol besides general anti-ageing effects and do not have comparable evidence. "Pregnancy-safe" claims are not substantiated and may expose brands to liability. This trend began with bakuchiol, a plant extract that claims to be similar to retinol based on gene expression profiling and an independent clinical trial, but the data presented are insufficient to make this claim.[39–41]

Despite a lack of robust evidence supporting efficacy in acne vulgaris, **hypochlorous acid sprays** have gained widespread popularity on social media as a convenient acne treatment option. Anecdotal reports of mild to moderate skin irritation have emerged among individuals who have adopted this trend inappropriately.

The 2021 TGA advertising amendments led to a surge in **makeup products marketed as secondary sunscreens**, likely to allow influencer testimonials in their marketing. While iron oxides offer benefits for pigmentation, makeup is generally inadequate as primary sun protection due to insufficient application and higher costs.

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The Role of Nutraceuticals in the Aesthetics Industry: Bridging the Gap Between Nutrition and Skincare

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OUTLINE: (i) Nutraceuticals are emerging as a significant adjunct to topical skincare and treatments, targeting skin health externally and from within.

(ii) This article examines the science behind nutraceuticals, their mechanisms of action, and their integration into cosmeceutical products and clinical practices.

(iii) Emphasis is placed on understanding the bioavailability, synergistic effects, and practical application of nutraceuticals for dermatologists seeking to enhance their treatment offerings.

KEYWORDS: nutraceuticals, skin health, anti-ageing, bioavailability, cosmeceuticals, anti-inflammatory, personalised nutrition, NAD+, collagen peptides, oxidative stress.

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Essential terminology

Nutraceutical:
A bioactive compound derived from food sources that provides health benefits beyond basic nutrition. Commonly found in supplements aimed at improving specific physiological processes.

Bioavailability:
The proportion of a nutraceutical that enters circulation when introduced into the body, thus having an active effect on target cells.

Synergistic effects:
The interaction between two or more nutraceuticals that results in a combined effect greater than the sum of their individual effects.

Gut-skin axis:
The relationship between gut health and skin health, influenced by the microbiota of both, and their impact on inflammation and immune function.

Introduction

Nutraceuticals are emerging as powerful tools in the aesthetics industry, where there is a growing focus on holistic approaches to skincare. Traditionally, skincare treatments have emphasised topical applications—creams, serums, and clinical procedures. However, integrating nutraceuticals offers a dual approach: treating the skin from inside *and* outside.

Recent advancements in nutraceutical science highlight the critical relationship between -nutritional health and skin vitality. Nutraceuticals, which encompass bioactive compounds derived from food sources such as vitamins, minerals, polyphenols, and omega-3 fatty acids (O3FA), can work at a cellular level to combat signs of ageing and skin disorders. This article will explore the biochemical mechanisms behind nutraceuticals, the evidence supporting their efficacy, and how dermatologists and skin professionals can integrate these products into their practices to deliver superior results.

Understanding nutraceuticals

Definition and scope

Nutraceuticals are products derived from food sources that offer additional health benefits beyond essential nutritional value. Unlike dietary supplements that primarily address nutrient deficiencies, nutraceuticals target specific physiological pathways, such as enhancing collagen production, mitigating inflammation, and boosting antioxidant defence mechanisms. Unlike pharmaceuticals, which aim to treat or cure specific diseases, nutraceuticals support and enhance the body's baseline biological functions, improving overall wellness.

In aesthetic medicine, nutraceuticals have gained attention for their ability to improve skin health. Bioactive compounds like vitamins, minerals, plant polyphenols, collagen peptides and O3FA are recognised for their potential to influence skin health span—supporting the skin's structure, elasticity, and resilience.

Historical context

The concept of using food-derived substances for health has historical roots that extend back thousands of years. Ancient civilisations used botanical extracts for skin and overall health. However, the term "nutraceutical" was coined in the 1980s, bringing a modern understanding to the field. Initially confined to general wellness, nutraceuticals have made their way into the aesthetic medical space. Research increasingly supports the connection between nutrition and skin concerns, with a significant focus on skin ageing. Over the past two decades, aesthetic clinicians have adopted nutraceuticals as an adjunct to traditional topical treatments, offering a holistic approach to enhancing skin health and combating age-related changes.

Scientific foundations

The effectiveness of nutraceuticals lies in their ability to target key biochemical and physiological pathways crucial for skin health:

- **Antioxidants:** Nutraceuticals like vitamin C and plant polyphenols resveratrol and quercetin neutralise reactive oxygen species that lead to oxidative stress and cellular damage, one of the main contributors to ageing skin.[1]
- **O3FA:** Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) fatty acids, derived from sources like fish or algal oil, play a crucial role in optimising the skin barrier and modulating inflammatory responses, aiding in conditions like acne, psoriasis, and eczema.
- **NAD boosters:** Nicotinamide riboside (NR), niacinamide and nicotinamide mononucleotide (NMN) enhance cellular energy production and DNA repair by boosting NAD+ levels, essential for maintaining skin cell vitality.[2]
- **Collagen peptides:** Hydrolysed collagen is now recognised as playing a significant role in enhancing dermal collagen quality and overall skin hydration.[3]

Nutraceuticals support the body's natural systems, such as the immune system, antioxidant pathways, and cellular regeneration processes, collectively contributing to healthier, more resilient skin.

Nutraceuticals and skin health

Mechanisms of action

Nutraceuticals work at the cellular level to improve skin health by addressing three primary mechanisms:

- **Collagen synthesis:** Collagen, the structural protein responsible for skin firmness, diminishes with age, leading to wrinkles and sagging skin. Nutraceuticals like vitamin C and hydrolysed collagen peptides have been shown to stimulate collagen production, helping restore skin elasticity and reduce visible signs of ageing.[3]
- **Antioxidant defence:** Skin is constantly exposed to environmental stressors such as ultraviolet (UV) radiation, climate extremes, harmful chemicals and pollution, all generating free radicals. Nutraceuticals polyphenols from green tea (quercetin and resveratrol) and coenzyme Q10 help neutralise these free radicals, protecting the skin from oxidative stress and delaying the ageing process.[1]
- **Anti-inflammatory pathways:** Chronic inflammation is a significant factor in every skin condition, including acne, rosacea, and psoriasis. DHA and EPA from O3FA derived from algal oil help reduce inflammation by modulating pro-inflammatory cytokines. Curcumin, a compound found in turmeric, also offers potent anti-inflammatory benefits, which are also shown to reduce skin redness and irritation.

Key nutraceuticals in supplements

Several nutraceuticals have garnered attention for their proven efficacy in enhancing skin health:

- **Vitamin C:** Essential for collagen synthesis, vitamin C has antioxidant photoprotective effects that help shield the skin from UV damage.
- **Hyaluronic acid:** Ingestible HA has been shown to improve skin hydration.
- **O3FA:** EPA and DHA from vegan sources like algal oil provide anti-inflammatory benefits for many

skin conditions and improve barrier function, skin hydration, and texture.

- **Polyphenols:** Found in green tea, resveratrol and quercetin are polyphenols known for their antioxidant properties that help mitigate free radical damage and optimise cell processes in the skin.[1]

- **Collagen peptides**: Unlike high molecular weight collagen protein molecules, these hydrolysed collagen peptides are bioavailable and have been shown to promote fibroblast activity, thereby enhancing collagen and elastin production.[3]

Synergistic effects

Combining nutraceuticals often results in a synergistic effect that enhances overall skin health. Examples include:

- **Vitamin C, hyaluronic acid, and collagen peptides:** Vitamin C not only directly supports collagen synthesis but also enhances collagen peptides' absorption, leading to improved skin structure and resilience. Hyaluronic acid also acts with collagen peptides to improve skin firmness and overall hydration levels.

- **NAD boosters and polyphenols:** Combining NAD+ precursors like NR with antioxidants such as resveratrol and quercetin offers a comprehensive approach to maintaining cellular energy, reducing the damaging impact of cellular senescence, and mitigating oxidative damage, thereby extending skin longevity.[1]

For skin professionals, understanding these synergistic effects is important in recommending nutraceutical supplements that work alongside topical formulations and treatments to address multiple layers of skin biology, ultimately elevating patient outcomes.

Integration in clinical practices

Formulation strategies

Incorporating nutraceuticals into supplements and skincare routines requires close attention to their formulation, particularly concerning bioavailability and stability—two critical factors influencing their effectiveness. Bioavailability refers to how effectively the body absorbs and utilises an active ingredient, which can vary significantly based on the form of the supplement. Stable encapsulation, hydrolysation, and liposomal delivery methods are commonly employed to enhance bioavailability, ensuring that nutraceuticals such as O3FA and collagen peptides reach the target tissues effectively.

Opportunities for clinical integration

Integrating nutraceuticals into dermatological practices presents an opportunity to create new revenue streams while enhancing patient satisfaction. To offer comprehensive treatment packages, skin professionals can combine nutraceuticals with clinical device modalities such as lasers, IPL, RF or microneedling. For example, pairing microneedling with collagen peptide supplementation can synergistically amplify collagen stimulation, improving skin texture and reducing wrinkle depth.

Nutraceuticals also offer support for long-term patient care. Anti-ageing supplements like nicotinamide riboside in combination with niacinamide complement skin rejuvenation treatments, while O3FA help manage inflammatory conditions like acne. This internal-external synergy improves patient outcomes and boosts satisfaction, fostering continued engagement with the practice.[2,4]

Product development and consumer education

Nutraceuticals are essential in developing products to address specific skin concerns, such as ageing, acne, sensitivity and other inflammatory concerns. Educating patients about nutraceuticals is critical to their successful integration into skincare routines. Dermatologists and skin professionals can lead by educating their patients on how these compounds can complement topical skincare and treatments and highlight the benefits of nutraceuticals for skin health.

Case studies: Combining cosmeceuticals with nutraceuticals for acne treatment

A 30-year-old patient suffering from inflammatory acne was advised to integrate an omega-3 supplement (derived from algal oil) with a standard topical retinoid regimen. Over 12 weeks, the patient experienced a significant reduction in inflammatory lesions and skin redness, highlighting the synergistic benefits of combining internal anti-inflammatory support with external retinoid application.[5]

A review of 38 studies was performed to identify the spectrum of uses for O3FA supplementation and evaluate the current evidence level for its clinical application in skin disease prevention and management. This review yielded many well-studied benefits of O3FA in dermatology. Given its high safety profile, low cost, and ease of supplementation, the authors of this study describe O3FA as a reasonable supplement that may benefit patients wishing to improve inflammatory skin conditions through diet. Areas of clinical interest where supplementation may be valuable include O3FAs for systemic UV photoprotection, as well as adjuvant treatment for acne to reduce both inflammatory lesion count and the severity of mucocutaneous side effects associated with Isotretinoin (prescription retinoid) use.[6]

In a 10-week, randomised, controlled trial, 45 participants with mild to moderate acne were divided into three groups: one receiving 2,000 mg of O3FA (EPA and DHA), another receiving 400 mg of gamma-linoleic acid (GLA) from borage oil, and a control group with no supplementation. Both the omega-3 and GLA groups showed significant reductions in both inflammatory and non-inflammatory acne lesions, with the omega-3 group demonstrating a greater decrease. Specifically, the omega-3 group experienced a 43% reduction in inflammatory lesions and a 20% reduction in non-inflammatory lesions, while the GLA group saw a 33% and 16% reduction, respectively. Acne severity grades also decreased significantly in the omega-3 group, dropping from 2.4 to 1.7, compared with the GLA group's reduction from 2.3 to 1.8. Cell biopsies from both groups revealed reduced levels of interleukin-8, suggesting lower inflammation. No severe adverse effects were reported. These findings indicate that omega-3 supplementation may be a more practical option for reducing acne severity through its anti-inflammatory effects.[7]

Future directions and challenges

Emerging trends in nutraceuticals

The future of nutraceuticals in dermatology practices likely lies in the personalisation of regimens. Advances in genomics and metabolomics have made it possible to tailor supplements based on an individual's genetic predisposition, lifestyle, and specific skin needs. For instance, patients with a genetic predisposition to higher oxidative stress may benefit more from a regimen rich in polyphenols and other antioxidants.

Optimising bioavailability

Optimising bioavailability remains a crucial focus in the development of nutraceuticals. Research into understanding stability, molecular interactions with cells and harnessing advanced delivery systems, such as nano-encapsulation and slow-release formulations, promises to improve the stability and absorption of compounds, thereby ensuring patients receive the full benefits of their supplements.

Challenges and considerations

Despite their potential, nutraceuticals face several challenges:

- **Regulatory issues:** The nutraceutical industry is regulated by standards different from those for pharmaceuticals. Compliance with guidelines, such as those set by the Therapeutic Goods Administration in Australia, is critical to maintaining patient safety.
- **Quality control:** There is a need for third-party testing and validation to ensure the quality and efficacy of nutraceutical products. Skin professionals may have difficulty confidently recommending products to their patients without stringent quality control.

The role of formulators and brands

Formulators and brands play a pivotal role in advancing the nutraceutical industry. Brands that base formulations on clinical trials and emphasise transparency, clean ingredient sourcing, and rigorous third-party testing will be at the forefront of delivering high-quality products to dermatologists. This collaboration is crucial to ensure that nutraceuticals can be integrated into clinical practice safely and effectively.

Essential nutraceuticals for skin health

- **NAD boosters coupled with antioxidants:** NAD+ boosters like nicotinamide riboside and niacinamide are essential for maintaining mitochondrial health and cellular energy, promoting DNA repair, and improving skin function. When paired with antioxidants like resveratrol and quercetin, these boosters provide comprehensive protection against oxidative stress and enhance overall skin resilience.[1]
- **Clinical Data:** A double-blind, placebo-controlled human trial with 113 participants showed that NR supplementation (500mg/day) resulted in a **90% increase in NAD+ levels after four weeks.** Resveratrol was also demonstrated in a six-month, triple-blind, placebo-controlled study to decrease oxidised LDL by 20% and apolipoprotein B by 9.8%, indicating cardiovascular benefits and systemic anti-inflammatory effects.[2,8]
- **O3FA from algal oil:** O3FA (EPA and DHA) are crucial in reducing inflammation and improving the skin barrier. Algal oil, a sustainable and vegan-friendly source, offers benefits similar to traditional fish oil without environmental impact.
- **Clinical Data:** A randomised trial showed that supplementation with EPA and DHA reduced UV-induced erythema and improved skin hydration and barrier function. A separate randomised controlled trial showed that **DHA supplementation from algal oil reduced serum triglyceride levels by 26%** and lowered cardiovascular disease risk factors. A further study demonstrated that EPA supplementation significantly improved atopic dermatitis symptoms.[5]
- **Collagen peptides:** High molecular weight collagen is not efficiently absorbed by the body; however, hydrolysed collagen peptides are bioavailable and stimulate endogenous collagen production, promoting skin firmness and elasticity.

- **Clinical Data:** Bioactive collagen peptides have been shown to **support skin elasticity, hydration, and firmness**. In a controlled study, individuals taking bioactive collagen peptides experienced a **13% increase in skin elasticity after 8 weeks and a significant reduction in wrinkle depth**.[9]

- **Prebiotics for gut health and the gut-skin axis:** Prebiotics support the gut microbiome, which significantly influences systemic inflammation and skin health. A balanced gut microbiome helps mitigate inflammatory skin conditions such as rosacea and eczema, emphasising the importance of including prebiotics in a holistic skincare approach.[10,11]

Conclusions

Nutraceuticals represent a promising frontier in dermatology, offering the potential to elevate skin health from within significantly. From NAD+ boosters that optimise mitochondrial health and combat oxidative stress to O3FA for reducing inflammation and collagen peptides for improving skin firmness and elasticity, these compounds provide potent benefits for preventive and corrective skin treatments.

As skin professionals continue to explore integrating nutraceuticals into their clinical practice, the importance of ongoing research cannot be overstated. Collaboration between biochemists, cosmetic chemists, and industry professionals will be crucial in advancing the development of scientifically validated bioavailable formulations that can transform the aesthetics and dermatological landscape. Nutraceuticals are poised to revolutionise how we approach the future of skin health by bridging the gap between internal health and external treatments.

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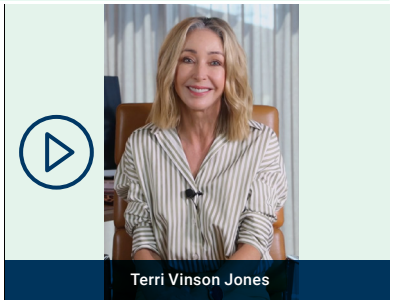
Topical Peptides, Growth Factors, and Exomes: Hype or Science?



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Disclosures: Terri Vinson Jones is the formulator and Managing Director of Synergie Skin. No reference is made to Synergie Skin formulations are made in this article.

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OUTLINE: This article outlines the scientific basis and applications of peptides, growth factors, and exosomes in skincare, highlighting their role in modulating cellular communication, anti-ageing, and wound healing. Peptides, short chains of amino acids, are versatile molecules that signal the skin to produce beneficial outcomes such as collagen production, barrier repair, and reduced inflammation. They are categorised into various types, including signalling, carrier, enzyme-inhibiting, and neuropeptides, each offering specific skin benefits.

Growth factors, larger proteins, stimulate processes like cell proliferation and wound healing but raise safety concerns, particularly regarding their potential to promote uncontrolled cell growth. Exosomes, a recent innovation, are extracellular vesicles that deliver complex cargo (e.g. genetic material, peptides, proteins) into receptor cells, offering promising results in skin regeneration and wound healing. However, like growth factors, exosomes require further research to confirm their safety and efficacy.

The article also addresses the challenges of skin penetration due to molecular size, outlining strategies like encapsulation, fragmentation, and clinical treatments to enhance delivery. In conclusion, while peptides, growth factors, and exosomes hold great promise in skincare, further studies are needed to fully understand their long-term effects and optimise their use in skin treatments.

KEYWORDS: peptides, growth factors, exosomes, cellular regeneration, cellular communication

Vinson Jones T. Topical peptides, growth factors, and exomes: Hype or science? Opin Prog Cosmet Dermatol. 2025;4(2):41–48.

Introduction

Peptides and topical growth factors have been marketing buzzwords for decades. These molecules highlight the synergy between skin cells and topical chemistry, offering more than just superficial results. Topical exosomes are a more recent addition to the aesthetics industry, emerging in the aesthetic sphere over the last decade.[1] This article will help to cut through the fake science marketing to understand how these molecules and entities influence skin cells through cell signalling and gene expression.

Topical peptides

What are topical peptides?

Peptides are short chains of between 2 and 50 amino acids that signal the body to produce specific molecules and biological outcomes. Oligopeptides consist of 2 to 10 amino acids and polypeptides consist of 10 to 50 amino acids. Any amino acid chain beyond 50 amino acids is considered a protein.[2]

What are the biological functions of topical peptides?

Peptides can successfully support, upregulate and often mimic other beneficial molecules in the skin and body to improve cell communication, regenerate, repair, and improve the appearance of the skin from the barrier to the deep dermal layer. Peptides can potentially treat numerous skin concerns and improve many

functions in the skin, including increasing collagen and hyperpigmentation and reducing cellular inflammation. Specific peptides, such as palmitoyl tetrapeptide-7, can modulate inflammatory pathways by downregulating TNF-α and IL-6 cytokines.[3]

How are peptides synthesised in the laboratory?

When it comes to laboratory-created peptides, the production possibilities are almost endless. Imagine the permutations of 20 amino acid groups in different-sized chains and in different combinations! More advanced technologies harness the production of synthetic peptides using advanced biotechnology via High Throughput Screening (HTS) technology. This involves creating computer-generated 'peptide libraries' whereby hundreds of thousands of amino acid sequences are generated. Each peptide sequence is specifically screened for its ability to mimic a specific biological function in the skin. This can include reducing inflammation, improving barrier function, increasing fibroblast activity, or reducing excessive melanocyte activity.

By decoding naturally occurring amino acid sequences, biomimetics can be incorporated into creating laboratory-synthesised peptides. Using the extensive peptide library and analysing the impact of specific amino acid sequences on the skin, scientists can create a detailed peptide structure that successfully interacts with human skin cells, enzymes, and receptors. Through computational design, biotechnology, and novel screening methods, laboratory-made peptides can be leveraged to create bespoke peptides targeting specific concerns to improve skin health, combat signs of ageing, improve wound healing, and address inflammatory skin conditions.[4]

Following the peptide modelling, they are rigorously tested for stability, human safety, efficacy, and effective delivery to target cells. We have come a long way from discovering the skin benefits of naturally occurring copper peptides in the 1970s.

Functions of peptides

Topical peptides can be categorised based on their specific skin functions and mechanisms of action. They provide a comprehensive range of skin benefits, including regeneration, anti-ageing, addressing inflammation, and cell repair.[5] The primary peptide categories include:

Signalling peptides
Send messages to skin cells to produce molecules for regeneration and repair. Palmitoyl pentapeptide-4, aka Matrixyl, has been shown to promote collagen production, improve elasticity and reduce the appearance of rhytids after several weeks of application.[6]

Carrier peptides
Deliver essential minerals (copper, calcium, magnesium) to the skin needed for crucial cell functions such as wound healing and reducing inflammation. An example is the copper peptide/ glycyl-L-histidyl-L-lysine, aka GHK-Cu.[7]

Enzyme-inhibiting peptides
Down-regulate enzymes such as matrix metalloproteinases (MMPs) that break down collagen and other structural proteins in the skin, thereby reducing wrinkle formation. Tripeptide-10 citrulline is an example.[8]

Neuropeptides
Directly impact nerve/muscle cell communication. These peptides can reduce dynamic muscle contraction to complement the effects of anti-wrinkle injectables or minimise expression lines.

Acetyl hexapeptide-8/ Argireline, which acts via inhibiting the SNARE complex, is involved in neurotransmitter release at neuromuscular junctions. This peptide can reduce dynamic muscle contraction and minimise the appearance of wrinkles.[9]

Anti-microbial peptides (AMPs)
It protects the skin from microbial insult, protects the barrier, improves skin immunity, and supports the skin microbiota. LL-37 is an important naturally occurring peptide produced by human skin cells. While it is not currently available as a topical skincare ingredient, specific postbiotic formulas can enhance the production of these naturally occurring peptides.[10]

Antioxidant peptides
Neutralise ROS, protecting skin from environmental damage, advanced glycation end products and premature ageing. Carnosine, a dipeptide, inhibits lipid peroxidation and helps reverse skin glycation.[11]

Anti-inflammatory peptides
Reduces inflammatory markers and addresses irritated skin. These peptides are recommended for sensitive skin and rosacea and address redness and irritation. For instance, acetyl hexapeptide-49 reduces redness, skin discomfort and sensitivity by reducing pro-inflammatory IL-8 cytokine release.[12] Further, acetyl tetrapeptide-40 inhibits pro-inflammatory mediators IL-6 and VEGF, both of which contribute to the exacerbation of facial redness and general skin inflammation. This peptide is particularly useful for addressing rosacea symptoms.[13]

Topical growth factors

Growth factors are complex proteins that are much larger molecules than their peptide counterparts. They play an essential role in processes such as stimulating regeneration, cell communication, regulating cell proliferation, wound healing, and repairing cells from environmental stressors.

Growth factors are primarily used to reduce visible signs of maturing skin, aid in wound healing, reduce abnormal scar formation, and modulate inflammatory responses (**Table 1**). They bind to cell membrane receptors, initiating intracellular signalling pathways within the cell to promote cellular activities.

Growth factors can be derived from multiple sources, including human cell types and plant sources, or they may be synthesised. However, growth factors exhibit less diversity in number and function compared with the versatility of topical peptides. Hundreds of thousands of peptide sequences can be laboratory-created for specific skin concerns, whereas the number of growth factors used topically is more limited.

Growth factors, being large proteins, do not penetrate the epidermis as effectively as short-chain amino acid peptides. They usually require chemical vehicles to penetrate target regions such as the dermis. Using biomimetic growth factors structurally similar to their human counterparts can also improve skin penetration,

Table 1. *Topical growth factors used in skincare and their impact on skin function.*

Growth Factor	Source	Primary Function	Impact on Skin
Epidermal Growth Factor (EGF)	Naturally occurring in the body	Stimulates cell growth and proliferation	Promotes skin healing, increases collagen production, and enhances the skin barrier. Helps reduce wrinkles and improve skin texture.
Fibroblast Growth Factor (FGF)	Derived from human fibroblasts, plants, or synthetically produced	Stimulates fibroblasts, which are critical for collagen production	Improves wound healing, increases skin elasticity, and aids in skin regeneration. Helps reduce fine lines and scars.
Platelet-Derived Growth Factor (PDGF)	Found in platelets and produced synthetically	Encourages tissue regeneration and cellular proliferation	Aids in wound healing, collagen formation, and promotes overall skin rejuvenation, contributing to firmer and smoother skin.
Transforming Growth Factor (TGF-β)	Found in various cells, including platelets and macrophages	Regulates cell growth and differentiation	Boosts collagen synthesis, improves skin elasticity, and helps reduce scarring. Also used for anti-ageing effects.
Vascular Endothelial Growth Factor (VEGF)	Found in blood vessels and created synthetically	Promotes blood vessel formation	Increases nutrient delivery to skin cells, promotes healing, and improves skin hydration and overall vitality.
Keratinocyte Growth Factor (KGF)	Secreted by fibroblasts	Supports keratinocyte (skin cell) proliferation	Enhances skin barrier function, accelerates wound healing, and helps in skin repair after damage.
Insulin-Like Growth Factor (IGF)	Produced naturally in the liver, or synthetically derived	Promotes cell growth, survival, and metabolism	Stimulates collagen synthesis, improves skin hydration, and enhances elasticity. Supports anti-ageing by improving overall skin structure.
Neurotrophins (NTs)	Naturally found in nerve cells and skin	Affects nerve cell development and survival	Helps maintain skin homeostasis, improves sensitivity, and can enhance skin repair and healing.

as they have a greater affinity for binding with natural receptors.

Human-derived exogenous topical growth factors may stimulate cell proliferation, raising concerns about the possibility of uncontrolled cell growth, potentially increasing the risk of tumour development. While this has not been conclusively proven in skincare products, there is anecdotal evidence of abnormal skin growths and a theoretical risk for growth factors used in a long-term skin regimen, particularly in those with a hereditary or preexisting risk of skin cancers.[14]

Growth factors derived from plants are less likely to pose a skin cancer risk compared with human growth factors. While they still support skin health, they do not bind to the same cell receptors as human growth factors and stimulate cell proliferation less directly. Their structure and mechanism of action make them less likely to promote tumour development, and their antioxidant properties may even reduce cancer risk. One study showed that certain soy-derived phytohormones can improve collagen production and inhibit elastin breakdown.[15]

While their efficacy is widely supported, it is important to remember that long-term studies are still needed to confirm the safety of topical growth factors, particularly with the extended use of human-derived proteins.

Exosomes

While growth factors have been very popular in the last decade, exosomes are an exciting new field in dermatology and aesthetic medicine and represent a new frontier in topical skincare.

What are exosomes?

Exosomes are small extracellular vesicles released by cells to facilitate intercellular and intracellular communication. They are formed within cells in structures called multivesicular bodies, which fuse with the recipient cell membrane to release the exosomes. Exosomes deliver liposomal-encapsulated packages of cargo, including DNA, RNA, mRNA, peptides, lipids, cytokines, numerous growth factors, and other proteins. The target cells then take up these bioactive molecules through various mechanisms, including endocytosis.

Once inside this target cell, the cargo encapsulated by the exosome can influence cellular processes by impacting cellular signalling pathways, regeneration, repair and gene expression. Exosomes are microscopic extracellular nanovesicles, typically 30–140 nm in diameter.[16] In a natural cellular environment, they are released by cells into the extracellular space, where they interact with other nearby cells.

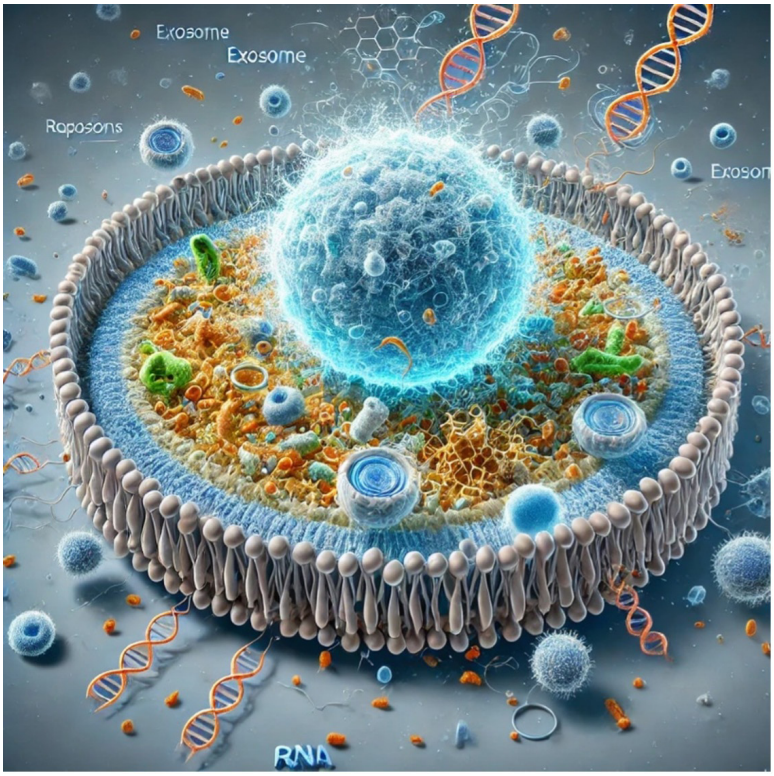

Figure 1. *A graphical representation of an exosome approaching and fusing with a lipid bilayer membrane of a recipient cell, releasing proteins, genetic material and lipids into the cell, influencing communication, gene expression and protein synthesis. Diagrammatic representation only.*

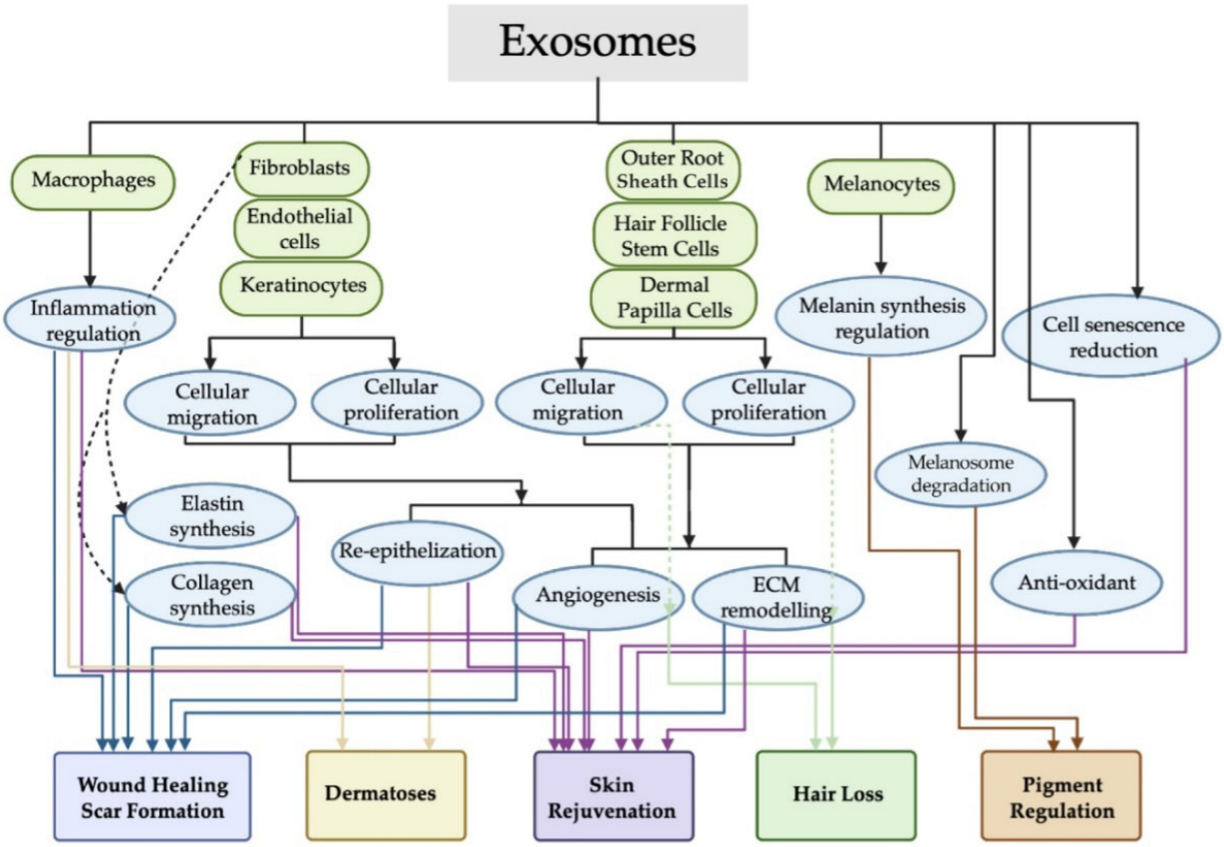

Figure 2. *Based on preclinical and clinical studies, the primary documented effects of exosomes in skin-related applications.*[19]

ECM, extracellular matrix.

Growth factors versus exosomes

Growth factors and exosomes have features in common. They are both involved in cellular communication to influence cell proliferation, differentiation and repair, but unlike growth factors that are individual proteins with specific functions, exosome packages are more complex (often containing growth factors themselves) and carry a broader range of regenerative and reparative molecules.

Dermatological benefits of exosomes

Topically applied exosomes have been shown to improve skin repair and wound healing, reduce inflammation, reduce rhytids through collagen stimulation, improve elasticity, increase hyaluronic acid synthesis, and reduce excess melanin synthesis. A relevant study demonstrates that topical exosomes derived from human umbilical cord mesenchymal stem cells accelerated the wound healing response, promoted angiogenesis, and upregulated collagen synthesis.[17] A more recent study by Lee et al. (2023)[18] highlights the ability of adipose tissue stem cell exosomes to promote wound healing outcomes and tissue regeneration.

Clinical applications of exosomes

Exosomes may be incorporated topically during clinical treatments such as skin needling, radiofrequency (RF), laser, fractional treatments, ultrasonic-assisted delivery, and chemical peels. A 2024 study by Rodriguez et al.[19] highlights the use of exosomes in medical aesthetics. They are also permitted for topical application in products for home use. However, the Food and Drug Administration in the US and the Therapeutics Goods Administration will only permit injectable exosomes once more human research is conducted.

Dermal penetration of exosomes

The precise mechanism of exosome penetration through the barrier has not yet been fully elucidated. Smaller exosomes <100 nm may penetrate the epidermis more easily. The vesicles' shape and lipid bilayer structure are thought to assist penetration. A study published in *Frontiers of Dermatology* by Kim, et al. (2017)[20] shows that human umbilical cord blood-derived mesenchymal stem cell exosomes take over 15 hours to fully penetrate the dermal layers to stimulate collagen and elastin production. Further, it is postulated that

exosomes utilise active transport mechanisms in the skin to aid their penetration rather than relying solely on passive diffusion.[21]

Plant-derived topical exosomes

There is also significant interest in plant-derived exosomes as vehicles as a novel form of inter-species signalling communication. Evidence shows that certain plant exosomes can deliver mRNAs, proteins, and metabolites that elicit responses in human skin cells. Plant-derived exosomes may also be considered a safer and more ethical alternative to mammalian-derived exosomes. In a recent study highlighting the topical application of Rosa Damascena, plant-derived exosomes were combined with microneedling to treat melasma in human subjects. Following four to five CIT/exosome combination treatments at 4-week intervals, the study demonstrated improvement in 90% of patients with negligible side effects. Improvements included reduced hyperpigmentation, increased collagen synthesis, and improved skin tone and texture.[22]

Safety concerns surrounding mammalian exosome use

The diverse cargo in mammalian exosomes depends on their origins. They are derived from multiple sources, including fat cells, bone marrow, platelets, umbilical cord, fibroblasts, and cloned mesenchymal stem cell lines.

There has been more recent concern over the quality of the exosome source. Exosomes should ideally be obtained from young, healthy cells that are free of chronic and acute disease. They must also be free from contamination and pathogens, and the batches must be homogeneous and stored correctly before use.

Human-derived exosomes may easily integrate into human host cells, and there is a risk of transmission of infectious agents and immunogenic activation. Most concerning is the need for long-term human independent clinical trials. There is also concern surrounding the risk of inducing abnormal cell growth, undesirable cell changes and possible tumorigenesis in the host.[23,24]

To mitigate risk, practitioners should verify the exosome source, ensure good manufacturing processes, handle the product correctly and adhere to the current regulatory guidelines.

Summary

Exosomes are the new kids on the block for cosmetic chemists. However, like many skincare trends, we need to tread carefully, particularly when using human-derived exosomes, and wait for more in vivo human trials data to be released. Human-derived exosomes in skincare are still in the early stages of research and development. While they show promise, more studies are needed to understand their safety, efficacy, and long-term benefits fully.

The problem of skin penetration: Peptides, growth factors and exosomes

When it comes to skin penetration, size matters. Generally, molecules with a molecular weight (MW) greater than 500 Daltons (Da) have difficulty penetrating the barrier. When considering peptides, growth factor proteins and multimolecular packages of exosomes, small peptides, will offer the best opportunity to penetrate.

Peptides over ten amino acids, growth factors and exosomes struggle to pass through the tight junctions of the stratum corneum effectively. Larger peptides, growth factors and exosomes can be too large to easily penetrate the stratum corneum and molecules of 50 amino acids are generally classified as small proteins. Type 1 collagen, for example, contains over 3000 amino acids, so I would NEVER formulate a topical product containing collagen.

However, the 'Dalton theory' based on MW is a general guideline, not an absolute law. The following strategies may also be harnessed to optimise penetration.

Formulation and application strategies to overcome the penetration challenges of peptides, growth factors and exosomes

Encapsulation with liposomes or other microparticles that can encapsulate peptides.

Clinical treatments such as micro needling, chemical peels, semi-ablative and ablative lasers, RF treatments, ultrasound, and electroporation will also enhance ingredient penetration.

Penetration-enhancing topical ingredients will increase skin permeability by temporarily disrupting the epidermal lipid matrix to enhance peptide delivery. Examples of gentle penetration enhancers include butylene glycol, dimethyl isosorbide and glycerine when used in conjunction with other enhancers.[21]

Occlusion with ingredients such as castor oil, lanolin, beeswax, squalane, carnauba wax, paraffin, and petroleum jelly can temporarily enhance permeability.[26]

Peptide and protein fragmentation to shorter amino acid chains (less than ten amino acids in general) can penetrate the stratum corneum more effectively.

Adding lipid ester groups (e.g., palmitoylation) to peptides and small proteins can increase their affinity

for the skin's lipid layers and improve penetration through the lipid bilayers.[25]

Harnessing nanoparticles (generally under 100 nm in size) of various organic and inorganic materials to carry larger molecules through the skin barrier.[27]

The future of peptide, growth factor, and exosome technology

Harnessing cutting-edge laboratory techniques shows great promise for bringing new peptides to market, exploring the biological action of growth factor proteins and expanding our understanding of how exosomes interact with skin cells.

There is ongoing research and development in exploring novel peptide sequences and formulations to enhance skin rejuvenation and address various dermatological concerns. This includes investigating new "smart peptides" that can adapt their function based on skin conditions.[28] As our understanding of peptide biology deepens, we can expect more targeted and effective peptide formulations that simultaneously address numerous skin concerns. Due to the sheer scope of their diversity, the versatility of peptides may allow for more bespoke skincare solutions tailored to individual skin needs and concerns.

Combination therapies are also an exciting new prospect in dermatology. Peptides, growth factors, exosomes, and clinical treatments can be combined to provide synergistic therapies and optimal patient outcomes.

With new technologies comes more evidence and some risks. While currently not TGA-approved as injectable treatments, more research could lead to more regulated exosome-based treatments. More clinical trials are expected to evaluate long-term human safety and efficacy, particularly regarding mammalian-derived growth factors and exosomes. Future research may also emphasise developing sustainable, ethical production methods, particularly when it comes to harvesting mammalian growth factors and exosomes.

Conclusion

Topical peptides, growth factors, and exosomes represent a convergence of cosmetic chemistry, clinical dermatology and skincare innovation, significantly impacting skin health through their ability to modulate cellular communication and repair processes. With their versatility and customisability, peptides have shown promise in addressing various skin concerns, from anti-ageing to inflammation. Growth factors, though shown to be effective, raise concerns due to their potential to promote abnormal cell growth.

Exosomes also offer promising results and represent a new frontier in dermatology through complex bioactive cargo delivery. However, animal-derived growth factors and exosomes necessitate further long-term research as new technologies require extensive human clinical trials to assess efficacy and safety concerns fully. As research continues, we anticipate more targeted, personalised skincare solutions that leverage these molecules and entities for optimal skin regeneration and repair while addressing safety concerns and regulatory oversight.

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Skincare and Social Media – Where Are We in 2025?

CLICK IMAGE TO LINK TO VIDEO DURATION_00:46

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OUTLINE: Advice around the use of skincare is sought after in many dermatologist consultations, whether for inflammatory skin disease, the aesthetic realm, or sun protection. The skincare industry is a multi-billion-dollar enterprise that is growing year on year. The public gains advice on using skincare from many sources, and there is a significant variance in expertise and knowledge. Social media is a prominent source of skincare information. Despite many dermatologists posting accurate and helpful guidance on skincare, cosmeceutical ingredients, and sun protection on social media, we still represent a relatively small proportion of those posting material regarding skincare in this realm. This article looks at the public's perception of current social media material regarding skincare and how dermatologists may enhance the current offerings and improve public knowledge about skincare.

KEYWORDS: skincare, social media, influencers, sun protection.

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Social media comprises numerous online platforms which allow two-way, real-time communication. It is used for entertainment, educational purposes, and marketing.[1] The use of social media in marketing is prolific, and it is now a mainstay in driving sales in the beauty industry. More than 5 billion people globally are active social media users.[1] This allows an opportunity for positive outcomes in terms of education on sun protection and appropriate skin care usage. However, there is also a downside to social media regarding skincare. The information disseminated by non-experts with abundant followings may be accepted as gospel by their audience, leading to adverse outcomes in some instances. The rise of "skinfluencers" in social media and marketing campaigns via product recommendations and advocating skincare routines can be incredibly influential in an individual's decision-making when it comes to skincare.[1]

Social media platforms commonly containing skincare content include Reddit, Instagram, Facebook, YouTube, Snapchat, Wibo, TikTok, and Tumblr.[2] A recent nationwide, online cross-sectional study targeting the general Saudi population sought to understand participants' social media behaviours and gather insights into decision-making about purchasing skincare products, cosmetic procedures, and makeup habits.[2] A total of 1,056 individuals were surveyed, and 67.9% of respondents identified as female. The consistent application of daily skincare across more than three body sites was associated with the regular use of social media platforms such as Snapchat ($p<0.001$), Instagram ($p<0.001$), and TikTok ($p=0.005$). Similarly, seeking advice from a dermatologist in the clinic ($p<0.001$), friends ($p=0.041$), or beauty influencers/advertisements on social media ($p=0.001$) was associated with a regular skincare routine.[2] Interestingly, in this survey population, 60% of females, but only 13.6% of males, applied sunscreen daily, compared with 90% and 45.7% who applied a facial moisturiser daily. Social media was ranked among the top three factors to consider when purchasing skin care products.[2]

A newly published study (also from Saudi Arabia) looked closely at the impact of social media on purchasing skincare and cosmetic products via an online questionnaire of 1,174 female participants.[3] Respondents ranged in age from 18 to the early 40s, with an average age of 22.5 years. Of note, 73.9% of respondents had a university level of education or higher. The authors aimed to identify the most used social media applications among participants, the sources of information they relied on regarding skincare and cosmetic products, and the level of trust in these sources.[3] Finally, this study assessed the effects of social media on the purchasing decisions of participants.

The most frequently used social media platforms in those surveyed were Snapchat (39.4%), TikTok (26.7%), Instagram (19.6%), Twitter (5.4%), YouTube (5.3%), and WhatsApp (2.6%). A total of 881 (75%) of the participating females reported using social media for more than an hour a day, 222 (18.9%) used it once or twice daily, only 45 (3.8%) used social media platforms once every few days, and 26 (2.2%) used it once per week.[3] A total of 51% of this study's participants became familiar with skin care products from social media platforms. Approximately 91.3% of the respondents' confidence in information related to cosmetic and skin care products was affected by visual presentation. This study further analysed the sources of information about cosmetic and skincare products on social media, 33.2% mentioned dermatologists, 26.8% mentioned friends/family, 20.1% mentioned social influencers, 14.4% mentioned cosmetologists, and 5.5% mentioned healthcare staff. A total of 95.4% expressed their trust in the information obtained from these sources, with 44.9% having an intermediate level of trust and 19.6% having a high level of trust.[3] Nearly half of the study respondents had purchased a skincare product recommended by an influencer on social media.[3] This study highlights the impact of information gained from social media in guiding users' purchasing decisions. The authors highlight that social media from non-experts tends not to elucidate that skin is individual and that a skincare routine should vary depending on many factors, including age, skin type, and any associated skin conditions.

With a user base of over one billion,[4] TikTok provides a means to create and watch short videos ("reels"). TikTok has become an important space to seek medical information, including in dermatology, particularly among young people. Recent overviews have indicated that medical misinformation is also prevalent in dermatology-related social media.[5,6]

In previous analyses on dermatology and TikTok, the rise of "skinfluencers" as a prominent source of skincare content has been evident. Some of these skinfluencers have bona fide credibility as dermatologists and cosmetic chemists.[5,6] However, others with no real expertise in dermatology or skincare create medically inaccurate content, recommending behaviours that can lead to adverse outcomes. A prime example in the skincare realm is the "highlighter method" of applying sunscreen to create a natural contour from tanning skin. In one video, the influencer applies a layer of low-SPF sunscreen all over her face, followed by a higher SPF product only on desired "highlights" before tanning. The premise is that "the sun will contour your face" naturally. Clearly, such behaviour carries risks of sunburn, skin malignancy and skin aging. SPF cocktails are another TikTok trend which encourages mixing make-up and/or skincare with sunscreen before application. Any time savings from this practice would be counter-balanced by the likelihood of diminishing the efficacy of the sunscreen from such a practice. "Beer-tanning" is another dermatology-relevant trend from the reels of TikTok, which touts beer as a "safe" way to tan.

Looking specifically at content creators in the #sunprotection space on TikTok, a cross-sectional study was undertaken over three consecutive days in August 2023 on TikTok. The investigators searched the following hashtags: #sunscreen, #sunprotection, #spf, #skincancer, and #skinprotection. The top 100 videos in each hashtag category were analysed. These videos were then categorised based on the type of content creator.[7] The categories of content creator included dermatologist, dermatology resident, non-dermatologist physician, physician assistant, nurse practitioner, registered nurse, aesthetician, patient/consumer, beauty blogger, skincare company, and others.[7] Of the 500 videos, only 16.6% were created by dermatologists. Beauty bloggers were the most prevalent creators in this analysis (38.7%), followed by patients/consumers (33.7%). Beauty bloggers were the top creators for most hashtags except for #skincancer and #spf. For #skincancer, patients/consumers (44%) were the top creators, with dermatologists comprising 39% of content creators. Beauty bloggers comprised only 1% of the #skincancer videos. For #spf, beauty bloggers and patients/consumers were tied for the top creators (33% each). Dermatologists created 18% of the #spf videos. For #skinprotection, #sunprotection, and #sunscreen, beauty bloggers were the most common creators.[7] Numerous studies have highlighted that most dermatology-related content on TikTok is not created by qualified dermatologists or other medical professionals.[8–11] The importance of accuracy in the skin cancer prevention space and the opportunity for healthcare professionals to use social media to educate the public cannot be overstated. This study illustrates that there is much for us to do.

Finally, the influence of social media on children and teenagers is a new area of huge concern when it comes to skincare. Ready access to numerous social media platforms means that our tweens and teens can readily be influenced by the latest skincare trends- even if they are not intended to be the target market. GRWM (get ready with me) reels on TikTok have led to many young girls becoming concerned about perceived imperfections and skin ageing. This has led to many adopting overly complicated skincare routines that are inappropriate for their skin. This results in irritant contact dermatitis and periorificial dermatitis, which are entirely preventable. After a significant backlash in the public domain over retailers perceived to be implicit in this trend, there has been much discussion in the media regarding the education of our young people and what is appropriate for their skin. In the absence of active skin disease, we know this to be daily sun protection and a cleanser and moisturiser, at most.

However, social media has a hold on its tween and teen audience, with high-end skincare being aspirational and about "fitting in" as much as the benefits for the user. It behoves us as dermatologists to perhaps embrace social media and assist with educating young people to embrace the healthy skin of this time of life and to protect it. Making sunscreen sexy will be a helpful part of this message.

There is no escaping the presence of social media in our world and its impact on our patients. Dermatologists currently account for a relatively small proportion of content on social media concerning skin health and skincare. As the foremost experts in skin health, dermatologists must have a more prominent role in educating the public about the appropriate use of skin care. Creating content is time-consuming and not for everyone. Whether we educate on social media or in the consulting rooms, we need to help our patients think critically about the content they imbibe and educate them that science and clinical experience count for much more than paid posts by influencers. To gain this confidence from the public, an increasing presence by dermatologists on social media will be crucial.

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Nanotechnology in Cosmetic Dermatology

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OUTLINE: Nanotechnology has revolutionised cosmetic dermatology, offering many benefits due to its unique physicochemical properties. Since its introduction in the mid-1980s, nanotechnology has been widely incorporated into various dermatological products, such as sunscreens, anti-ageing and local anaesthetic products. However, while it offers significant potential in cosmetic dermatology, concerns remain about its safety, particularly regarding systemic absorption, long-term toxicity and environmental impact. As nanotechnology continues to expand, further research is critical to fully understand its safety profile and establish appropriate guidelines for its safe, responsible application in cosmetic dermatology.

KEYWORDS: nanotechnology, nanomaterials, cosmetics, nanoparticles, cosmeceuticals.

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Introduction and background

Nanotechnology involves using nanoparticles or nanomaterials ranging from 1 to 100 nanometres (nm) and has significantly advanced cosmetic dermatology due to its remarkable physicochemical properties. Richard Feynman, often regarded as the 'father of nanotechnology,' initially introduced the concept of manipulating molecules and atoms to create components so miniscule they are invisible to the naked eye in the 1950s.[1] In 1974, Professor Norio Taniguchi formally defined 'nanotechnology' as the process of separating, consolidating, and deforming materials atom by atom or molecule by molecule.[2] The first use of nanotechnology in cosmetic preparations was by Christian Dior in 1986 with its anti-aging cream, Capture™, which used liposomes for better moisture delivery.[3] That same year, Lancôme launched its first nanotechnology-based product, Niosomes, followed by 'Plentitude Revitalift' in 1998.[4] Since then, many cosmetic companies have incorporated nanomaterials into their products (**Table 1**).

Nanotechnology offers numerous advantages for drug delivery. Firstly, the nanoscale size of the particles allows for a higher surface-to-volume ratio, which enhances the exposure of active molecules per dose administered to the stratum corneum.[5] Secondly, the size enhances material dispersibility, improving skin absorption, providing sustained release, increasing bioavailability, and increasing active ingredient delivery to targeted sites. Additionally, nanomaterials can stabilise cosmeceutical compounds that might otherwise degrade due to oxidation or other factors. In summary, nanotechnology offers greater bioavailability, sustained release, and improved tolerance and stability of active ingredients in skincare formulations.

Nanomaterials in cosmeceuticals

The cosmeceutical industry utilises various nanotechnologies, which can be categorised into organic and inorganic nanoparticles (**Figure 1**).

Organic nanoparticles are non-toxic, hydrophilic, biocompatible, and highly stable, making them ideal for lipid-based nanocarriers used in formulating active ingredients as carriers and absorption enhancers. These include liposomes, niosomes, solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), and nanoemulsions.

In contrast, inorganic nanoparticles, made of metals and their oxides, are often used in products that act on the skin's surface, such as gold and silver nanoparticles in antimicrobial products or nanoparticles of titanium oxide (TiO_2) or zinc oxide (ZnO) in sunscreens.

Clinical applications relevant to the skin and cosmetic dermatologists

Preventative skin care – Sunscreen formulations

Photoprotection against UV radiation is crucial to prevent cutaneous malignancies and photo-ageing.

Table 1. *Commercially available nanocosmeceutical formulations with their benefits.*

Product type	Nanotechnology	Benefits	Product name
Sunscreen	Inorganic particles (TiO_2 and ZnO nanoparticles)	Hydrophilic, biocompatible, safe and photostable Absorb UV light Transparency	• Eucerin Sun Lotion for Dry Skin – Beiersdorf AG • Daylong – Galderma
Retinoids	Nanosomes	Increased penetration and stability of their components	• Revitalift – L 'Oreal • Multi-Targeted Elixir – Re:Erth • Retinol Fix Blemish Gel Treatment – Nip+Fab • Dragon's Blood Hyaluronic Night Cream – Rodial
Moisturising and anti-aging nanomaterials	Nanoliposomes	Amphiphilic and increased skin penetration	• Capture Totale – Dior • Advanced Night Repair Protective Recovery Complex – Estee Lauder • Serum Night Repair – Estee Lauder • Moisture Liposome Eye Cream – Decorte • Sparkling Glacier Complexion Mist – Aubrey Organics • C-Vit Liposomal Serum – Sesderma • Rehydrating Liposome Day Crème – Kerstin Florian Skincare • Liposome Face and Neck Lotion – Clinicians Complex
	Niosomes	Increased efficiency, penetration, bioavailability and stability of drugs	• Niosome+ Perfected Age Treatment – Lancome • Eusu Niosome Makam Pom Whitening Facial Cream – Eusu • Anti-Fatigue – Moller for Man • Nio-Cell – Bellezza Italiana • Mayu Niosome Base Cream – Laon Cosmetics • Anti-Age Response Cream – Simple Man Match
	SLNs and NLCs	Increased shelf life Adheres to skin surface, forming an invisible occlusive film that prevents water loss	• Allure Body Cream – Chanel • Cream Nanorepair Q10 – Dr. Rimpler GmbH • Soosion Facial Lifting Cream SLN technology – Soosiun • Phyto NLC Active Cell Repair – Sireh Emas
	Gold and silver nanoparticles	Multiple and not fully elucidated anti-ageing actions, e.g., antioxidant effect	• Nano Gold Firming Treatment – Chantecaille • Nano Gold Energizing Eye Serum – Chantecaille • Cor Silver Soap – Cor • The Silver Anytime Moisturiser – Cor • Nano Gold Foil Liquid – LR Zeitgard • O3+ 24K Gold Gel Cream – O3+ • Orogold 24K Nano Ultra Silk Serum – Orogold
	Nanoemulsions	Transparent and stable	• Skin Caviar – La Prairie • Coco Mademoiselle Fresh Moisture Mist – Chanel • Bruma De Leite – Natura • Benpanthol Facial Cream Ultra Protect – Bayer Healthcare • Nanovital VITANICS Crystal Moisture Cream – Vitacos Cosmetics • Coni Hyaluronic Acid and Nanoemulsion Intensive Hydration Toner – Coni Beauty

NLC, nanostructured lipid carriers; SLN, solid lipid nanoparticles; TiO_2, titanium dioxide; ZnO, zinc oxide.

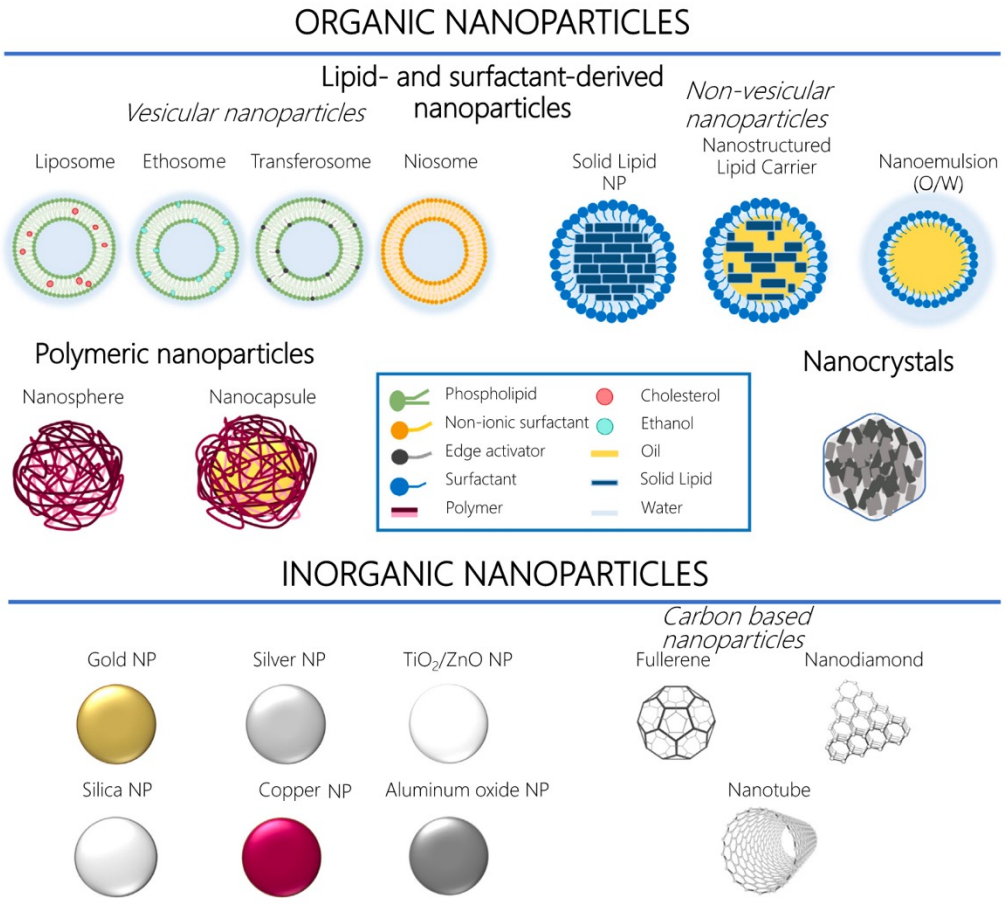

Figure 1. *Schematic representation of nanotechnologies used in cosmeceuticals. Adapted from Salvioni* et al. *(2021).*[5]
NP, nanoparticle; TiO_2, titanium oxide; ZnO, zinc oxide.

Traditional sunscreens often suffer from greasy application, chemical odour, and chalky appearance. Nanotechnology-based formulations overcome these issues, offering "sheer" or "invisible" sunscreens with better cosmetic results. When formulated as nanoparticles, TiO_2 and ZnO particles, commonly used in sunscreens, offer a higher sun protection factor (SPF) and improved cosmetic appeal due to their transparency. Additionally, carriers like SLNs and NLCs can act as physical UV blockers, enhancing the efficacy of sunscreen particles and reducing the amount needed.[6] Some products may incorporate silica nanoparticles in sunscreens for their mattifying effect, pore minimisation, and spreadability.[7]

Priming of skin pre-treatment – Retinoids

Retinoids are commonly used in anti-ageing products. However, their use is limited by low penetration and side effects such as pruritus and burning sensation at the application site, erythema, dryness, and photosensitivity.[8] They are also easily photodegraded by heat, air, or light exposure, leading to a rapid decline in efficacy, whether on the shelf or in the epidermis.[8,9]

In recent years, there has been increasing research into SLNs as carrier systems for retinol. Their advantages include UV blocking properties, which effectively protect against chemical degradation, and their nano-size allowing close contact with the stratum corneum, thus increasing the penetration of retinol into the skin.[10] They also form an occlusive layer on the skin, reducing trans-epidermal water loss, decreasing corneocyte packing, and enhancing drug transport.[11] Modified release formulations may also allow for controlled release of retinol, reducing irritation side effects.[12,13] Retinol-loaded SLNs have enhanced thermal stability by suppressing oxidation and reducing irritation through electrostatic repulsion, preventing aggregation among lipid nanoparticles.[14] Additionally, application to porcine skin showed increased epidermal thickness compared with retinol alone, suggesting potential clinical benefits.[14]

Clinical trials on nanoemulsion gel formulations of retinoids indicate these are more effective and better tolerated for acne vulgaris than conventional formulations. In one phase IV randomised controlled

trial (RCT), the tretinoin (0.025% w/w) nanoemulsion gel formulation was found to be significantly more effective in reducing total and inflammatory acne lesions, as well as having significantly less local adverse events than the conventional gel formulation.[15] Similar benefits were found when using a nanoemulsion gel combining adapalene and 1% clindamycin in another randomised open-label phase IV RCT.[16] Currently, nanoemulsion gel formulations of retinoids such as Retin-A Micro (tretinoin) gel microsphere (Bausch Health) are available in the United States. However, there is no commercially available formulation available in Australia.

Preparation of skin on procedure day – Local anaesthetic delivery

Transdermal delivery of local anaesthetic via liposomes is a promising advancement in needle-free pain management. Liposomes made of unsaturated phospholipids dissemble upon skin application, allowing their components to rapidly and deeply penetrate the stratum corneum and have a prolonged duration of action.[5] Liposomal-encapsulated tetracaine has demonstrated a superior topical anaesthetic effect over a eutectic mixture of local anaesthetics (EMLA) patch in two separate comparative studies.[17,18] In Australia, LMX4 (Dermocosmètica) is approved by the Therapeutic Goods Administration (TGA) and available commercially as a topical anaesthetic cream containing 4% lignocaine. It is applied to intact skin 30 minutes before a procedure, with an anaesthetic effect lasting approximately 60 minutes. Extemporaneously compounded local anaesthetic creams can provide superior penetration and efficacy due to the use of 'Lipoderm' (PCCA) base, with tetracaine (4–7%) and lignocaine (6–23%). However, care must be taken with these formulations as application over large areas may produce systemic toxicity. Additionally, since Lipoderm is water-based, if using lasers that target water as the primary chromophore, such as erbium (2,940 nm) and carbon dioxide (10,600 nm) lasers, anhydrous bases may be preferred.

Post-cosmetic treatment care – Retinoids, wound care, lightening and anti-ageing compounds

Nanotechnology plays a crucial role in post-cosmetic treatment aftercare and maintenance. As previously mentioned, retinoids play a key role in skin priming and maintenance. In wound healing, nanofibers promote cellular proliferation and wound closure, whilst antimicrobial agents such as silver nanoparticles in wound dressings help prevent infection.[5]

Nanotechnology has been used in the delivery of depigmenting topical agents such as hydroquinone,[19,20] azelaic acid,[21,22] kojic acid,[23,24] and tranexamic acid.[25,26] They are used in the prevention or treatment of post-inflammatory hyperpigmentation. However, their use is limited by adverse effects such as irritant dermatitis, characterised by erythema, pruritus, and desquamation, primarily due to their poor permeability through the stratum corneum, resulting in surface accumulation.[27]

Hydroquinone oxidises rapidly and has limited skin penetration due to its hydrophilic structure. Encapsulation of hydroquinone in SLNs protects it against oxidation and has improved penetration in rat skin.[19] The use of NLCs loaded with azelaic acid has allowed for the gradual release of the drug and reduced the rate of adverse effects.[21] Similarly, loading kojic acid into SLNs and NLCs has enabled this highly hydrophilic compound to bypass the stratum corneum effectively, resulting in enhanced tyrosinase inhibition and antioxidant activities compared with pure kojic acid.[23,24]

Alternatively, nanocrystals have been explored as a potential delivery method due to their ability to increase the drug's solubility and dissolution rate, resulting in improved bioavailability in the skin. For example, the crystallisation of hydroquinone in cellulose nanocrystals has been shown to allow sustained release, increasing its efficacy while simultaneously reducing adverse effects.[20] Similarly, the encapsulation of azelaic acid in nanocrystals has shown better skin bioavailability than conventional formulations.[22]

Anti-ageing compounds, such as antioxidants, vitamin C, and coenzyme Q10, have been incorporated into nanocarriers because the nanocarrier provides enhanced penetration of the active ingredient through the skin barrier.[5] Nanoparticles such as SLNs also provide superior stability and controlled release of the active agent, resulting in superior efficacy with lower irritancy.

Safety considerations and current regulatory guidelines

The safety of nanoparticles is a highly controversial topic. Although nanomaterials may be present in formulations as active ingredients or carriers, their use and role in marketed cosmetics generally are not widely advertised due to the current debate around the potential long-term toxicity of these nanoparticles in terms of health and the environment.

Health considerations

Ironically, the very advantage of nanoparticles—their nano-size—also poses a toxicity risk. Their small size raises concerns about systemic circulation and cellular entry.[28] Theoretically, penetration of the stratum corneum could occur via aqueous pores (diameter range: 0.4–36nm), via the intercellular lipid matrix (range: 5–7mm) or via the follicles (10–210 µm)

depending on the size of the nanoparticle.[5] Once in the dermis, the concern is that these nanoparticles may have higher chemical reactivity due to their increased surface-to-volume ratios and produce reactive oxygen species that can damage DNA.[28] For instance, TiO_2 nanoparticles at 20 nm have been shown to damage cellular DNA, even at low doses and without UV exposure.[29] However, there are other chemicophysical factors to be considered in predicting the penetration ability of nanoparticles, such as their composition, charge, and duration of retention in the stratum corneum.[5] Skin penetration studies have demonstrated that TiO_2 is safe when applied to intact skin, as it does not penetrate beyond the stratum corneum. The main concern arises when TiO_2 is used on broken skin, such as in acne, eczema, or wounds.[30]

Another concern is exposure via inhalation, as particulate air pollution is well known to cause acute increases in morbidity and mortality rates.[28] Studies have shown that particle size influences the site and amount of particle deposition, as well as subsequent mucociliary clearance, with toxicity considered higher for ultrafine particles.[28] Inhalation of high concentrations of nano-sized ZnO has been shown to result in a mild acute rise in inflammatory systemic biomarkers; however, the clinical significance of this is unclear.[31] Regardless, Shiseido formulates nano-TiO_2 and ZnO in wet-based products but avoids their use in aerosols to mitigate inhalation risks.

Environmental considerations

Inorganic nanoparticles, such as gold, titanium, and silica-based nanoparticles, are insoluble and unlikely to degrade after topical application.[32] When these particles are released into the sewerage systems, they may pose environmental risks, particularly to marine life. For instance, in laboratory studies, TiO_2 nanoparticles have been reported to inhibit algae growth, though real-world tests on this environmental impact are still lacking.[33]

Currently, there is limited information on the environmental risks of manufactured nanoparticles. Only a few studies have been published on nanomaterials' direct and indirect impacts, indicating a need for extensive research to evaluate their interactions with biological systems and ecosystems.

There is no single regulatory authority overseeing the use of nanoparticles. In Australia, only TGA-approved ingredients can be used to manufacture these products. However, the Food and Drug Administration does not require approval for cosmetic products and their ingredients before marketing in the United States. Manufacturers are encouraged to review the safety data of specific ingredients or comparable formulations to determine the safety of nanocosmeceuticals.

Conclusion

Nanotechnology has led to significant advancements in cosmetic dermatology, providing improved drug delivery systems and enhancing the efficacy and safety of active ingredients. However, nanoparticles have potential toxicity risks due to their small size and reactivity. Environmental concerns also exist regarding the impact of inorganic nanoparticles on marine life and ecosystems. Overall, further research is needed to establish precise guidelines for the manufacturing, advertising, nanotoxicology testing, and safe use of nanotechnology in cosmetic dermatology.

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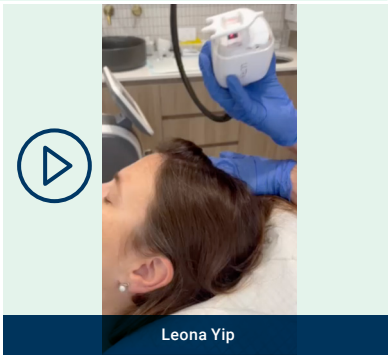
KeraLase™ Laser-assisted Delivery of Kerafactor™ Nanoliposomal Growth Factor Serum Treatment for Hair Regeneration



CLICK IMAGE TO LINK TO VIDEO DURATION_01:57

Leona Yip[1]

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Disclosures: Consultant, KOL or Advisory Board Member for CryoMed (Kerafactor), L'Oreal Australia, Galderma, Eli Lilly, Pfizer, Leo Pharma

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OUTLINE: KeraLase™ Laser-Assisted Delivery of KeraFactor™ Liposomal Growth Factor Serum can be used as a stand-alone hair rejuvenation treatment, or as adjunct to medical therapies for female pattern hair loss and male androgenetic alopecia to improve hair regrowth potential.

KEYWORDS: Hair loss, alopecia, hair growth, female pattern hair loss, androgenetic alopecia

L Yip. KeraLaseTM laser-assisted delivery of KerafactorTM nanoliposomal growth factor serum treatment for hair regeneration. Opin Prog Cosmet Dermatol. 2025;4(2):58–59.

Suitable conditions for treatment

- **Male androgenetic alopecia**
- **Female pattern hair loss**
- **Maintenance after hair transplantation**
- **Hair rejuvenation and revitalisation**

This treatment is best used as an adjunct to accompany medical treatments to optimise results. It may be used as monotherapy in early-stage hair loss in selected patients, but with less reliable efficacy and significantly higher costs than medications.

Possible risks

- **Mild scalp redness and mild stinging (less than 24 hours)**
- **Allergic reaction to Kerafactor™ product applied**
- **Infection (rare)**
- **Analgesia**

No analgesia is required. Treatment is comfortable and feels like mild tingling or pin pricks on the scalp.

Technique

This treatment can be delegated to a trained laser therapist. A course of 5–6 treatments is recommended with treatments performed every 4–6 weeks, followed by a medical review to decide on whether maintenance treatments could be beneficial.

Draw up the 6 ml of Kerafactor™ serum from the vial into 1 ml syringes using an 18-gauge draw up needle. Leave the draw up needles intact on syringes to deliver serum onto scalp after laser.

I use the Lutronic LaseMD Ultra non-ablative laser system (1927 nm thulium laser) to create scalp micro-channels that assist in trans-epidermal absorption of the Kerafactor™ serum into the scalp. Laser settings used are as recommended and published by the manufacturer:

- **Comb Tip, Static Mode**
- **200 µm spot size**
- **5 mJ of energy and 5 W of power**
- **2 Passes**

Treat desired areas on the scalp with laser handpiece using above settings, parting hair every 2–3 cm apart with fingers to expose scalp area for lasering. You can use combs to part the hair, but this is more time-consuming. This step takes approximately 10 minutes.

Immediately following laser treatment, apply Kerafactor™ serum droplets onto pre-lasered scalp areas using the 18-G draw up needle attached to the syringes. Then, massage scalp vigorously to help with absorption.

I advise patients to avoid hair washing for 24 hours after treatment.

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Neocollagenesis to Reduce Skin Laxity: A Review of the Mechanisms and Efficacies of Modern Devices

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OUTLINE: With an ageing population, dermatologists have observed a rise in the popularity of skin tightening procedures. Skin laxity, an inevitable manifestation of the natural ageing process, profoundly affects psychosocial factors, including self-confidence and even employability. For these reasons, skin laxity has become an important area of research and innovation. Several devices have sought to curtail the ageing process by stimulating neocollagenesis through physical, thermal, or ultrasound energy. We review the mechanisms and efficacies of non- or minimally-invasive technologies that target skin laxity, including radiofrequency, broadband infrared light, high-intensity focused ultrasound and micro-focused ultrasound, synchronous ultrasound parallel beam, rapid acoustic pulse™ technology, dermal Micro-Coring® technology, high-intensity focused electromagnetic field, and electromagnetic energy. The majority of these devices are safe for the skin of colour, especially with the use of test spots to ensure patient satisfaction and insulated probe tips when applicable. Looking ahead, elastogenesis is an important area of research in enhancing skin tightening technologies.

KEYWORDS: skin laxity, radiofrequency, radiofrequency microneedling, high-intensity focused electromagnetic field, high-intensity focused ultrasound, skin of colour.

Brown AB, Rawitscher CH, and Teller CF. Neocollagenesis to reduce skin laxity: A review of the mechanisms and efficacies of modern devices. Opin Prog Cosmet Dermatol. 2025;4(2):60–66.

Introduction and background

With an ageing population, dermatologists have observed a rise in the popularity of skin tightening procedures. Skin laxity, an inevitable manifestation of the natural ageing process, profoundly affects psychosocial factors, including self-confidence and even employability.[1] For these reasons, skin laxity has become an important area of research and innovation.

Skin laxity and the ageing process are closely associated with collagen. As we age, collagen loss accelerates as collagen regeneration declines. To understand how modern devices target skin laxity, we must review its pathology. At the macroscopic level, signs of laxity arise from the gradual detachment of the skin and adipose tissue from the underlying fascia, bone loss, and muscle and adipose atrophy.[2] Microscopically, as we age: 1) collagen becomes calcified; 2) advanced glycation end-products (AGEs) cross-link collagen; 3) glycosaminoglycans (GAGs), the disaccharides that link collagen fibrils together to form strong collagen become less sulfated and shortened; and 4) matrix metalloproteinases (MMPs), responsible for collagen degradation and extracellular matrix (ECM) homeostasis during times of skin healing, increase expression secondary to chronic oxidative stress.[3]

Several devices have sought to curtail the ageing process by stimulating neocollagenesis through physical, thermal, or ultrasound energy. Targeted damage by the devices initiates a wound repair response that activates fibroblasts and inflammatory mediators to promote neocollagenesis and activate matrix proteins.[4] For example, collagen III, the first collagen type to form at the site of traumatised skin, is eventually replaced by collagen I. Collagen I provides the tensile strength necessary for the mechanical

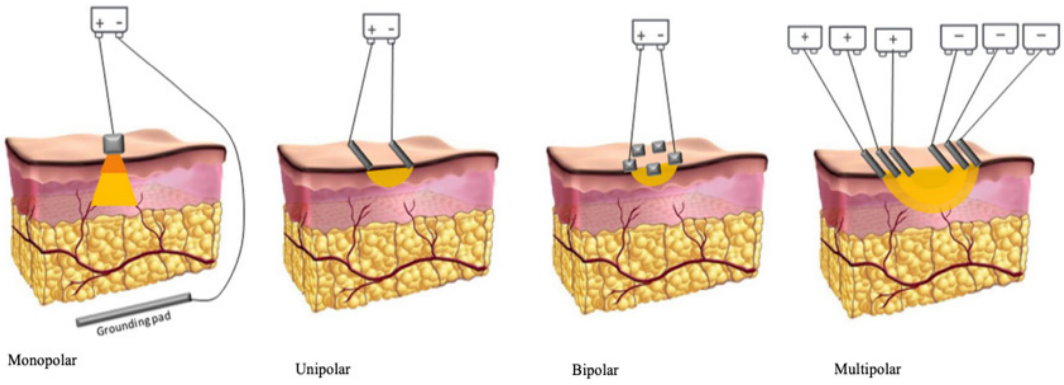

Figure 1. *Radiofrequency devices have four unique electrode configurations: monopolar, unipolar, bipolar, or multipolar. Figure courtesy of Dr. Michael Gold.*

stability of the skin. Collagen III, a thinner and less durable collagen type, provides elasticity to the skin and plays a crucial role in skin rejuvenation.[4] Collectively, newly formed collagen I and III synergistically enhance the strength and flexibility of the skin, leading to tissue tightening and a desired aesthetic outcome.

Skin of colour is often underrepresented in cosmetic clinical studies. Though all skin types share similar features of ageing patterns, darker skin types may require a different treatment approach or device to achieve the desired response. Caution is advised in devices that may lead to thermal injuries, scarring, or hyperpigmentation; providers may want to trial a device with a test spot on patients with darker skin types before committing to full treatment.

Radiofrequency

Radiofrequency (RF) devices treat skin laxity by using heat to initiate a healing cascade.[5,6] When the dermal tissue is heated, heat-shock proteins (HSPs) trigger fibroblasts to remodel collagen by destroying old, dysfunctional collagen and facilitating the formation of new collagen fibres. Specifically, HSP-47 is a protein found in the endoplasmic reticulum that facilitates the synthesis of collagen I molecules by tissue fibroblasts.[5,6] Since heating the skin may be uncomfortable for patients, many RF devices incorporate cooling mechanisms to penetrate the deeper dermal and subcutaneous fat layers while safeguarding the superficial layers of the skin from excessive heat. The cooling mechanisms enhance precision during the wound healing process and patient comfort.[7]

There are four types of RF devices: monopolar, unipolar, bipolar, and multipolar. Each type represents its respective number of electrodes and the manner in which energy is delivered to the intended target tissue (**Figure 1**).[8] Monopolar and unipolar RF devices, for instance, utilise a single electrode. Bipolar devices employ a single RF generator, allowing current flow between two electrodes. Multipolar devices utilise several RF generators.[6] Though both monopolar and unipolar devices incorporate robust epidermal cooling measures to safeguard the integrity of the skin's outermost layer, they are associated with increased discomfort compared to their counterparts. Alternatively, bipolar and multipolar RF devices act more superficially and thus require more treatment sessions to achieve comparable results, though a relatively less painful experience.[8]

Theoretically, RF is considered safe to use on skin of colour because it should only target the dermis, not the epidermis.[9] However, some RF devices have known adverse effects, such as scarring, hyperpigmentation, and thermal injuries. Insulated probe tips are safer for skin of colour.

Monopolar RF

The first RF tissue tightening device in the United States was Thermage ThermaCool®, a monopolar device. Unfortunately, numerous patients reported significant pain during the procedure and some required sedation. Adverse effects such as fat necrosis and atrophic scarring were also noted. To enhance patient comfort and reduce procedure duration, a newer device model, ThermaCool NXT®, was developed. This advancement introduced the Comfort Plus Technology (CPT) tip, which provided patients with a massage-like experience combined with radiofrequency energy.[7] In one study of 62 participants who used Thermage® to treat fine lines of the periorbital area, 83.2% showed softer lines, and 64.6% showed one Fitzpatrick point improvement at 6-month post-procedure photographs. Of the 33 participants who used Thermage® for a brow lift, 66.4% had an improved lift greater than the detection threshold (0.5 mm) in their 6-month post-procedure photographs. Notably, 50% of participants reported they were "neutral" or "unsatisfied" with their

outcomes, and only 10% were "very satisfied."[10] These patient-reported outcomes were similar to those of another study of 86 participants, in which 50% and 46% saw no difference in their skin tightness and appearance, respectively.[11]

Unipolar and bipolar RF

Other RF devices have been developed to address skin laxity and the discomfort associated with previous monopolar generations. Syneron's Polaris™ and ReFirme™ are bipolar RF devices incorporating light and RF energy. The synergistic effect of these two types of energies reduces the RF energy required for collagen denaturation and remodelling. Some devices utilise a vacuum apparatus with a bipolar RF system to deliver targeted RF energy to specific areas within the deep dermis. This modality necessitates less RF energy, resulting in better patient comfort.[12] Some devices employ both unipolar and bipolar modalities; the bipolar RF energy utilises superficial heating, while the unipolar energy allows for deeper dermal heating.[13]

Multipolar RF

The Venus Legacy™ by Venus Concept is a multipolar RF device that combines multipolar RF technology with pulsed electromagnetic fields. This modality stimulates fibroblast proliferation, angiogenesis, and new collagen fibres to improve skin laxity. EndyMedPro™ is another multipolar device that uses unique RF technology called 3DEEP™. This device incorporates six independent phase-controlled RF generators connected to multiple electrodes, each generating its electrical field. The individual electric fields repel one another, resulting in energy penetrating even deeper into target tissues. Consequently, the dermis is effectively targeted all while the epidermis remains protected, thereby enhancing overall patient comfort during the treatment.[14]

RF microneedling

Several devices have combined RF with microneedling to treat skin laxity and cellulite (**Table 1**). Rather than applying RF energy to the cutaneous surface, RF microneedling (RFMN) targets dermal and subcutaneous tissue via an electrode needle. Several passes at multiple depths should be treated to achieve the best outcomes. Because RFMN is a minimally invasive procedure, patient comfort is critical; topical anaesthetic or inhaled nitrous oxide often enhances patient experience. Before initiating treatment, however, all topical anaesthetic must be completely removed from the skin to avoid the products entering the skin and causing skin irritation. One study assessed the optimal temperature

Table 1. *Comparison of radiofrequency microneedling devices. Table courtesy of MRP®.*

Specifications	Jeisys Intracel	Inmode Morpheus 8	Lutronic Genius	Cutera Secret RF	Cynosure Potenza	ShenB Vivace	Scarlet SRF
Pin Energy (max) (mJ)	5100	Unknown	Unknown	Unknown	5099	799	Not specified
Power (max)	50W	65W	50W	25W	50W	36W	260 V, 60 Hz
Firing Time	10–50,000 ms	Up to 2 pps	10–1,000 ms	50–950 ms	10–50,000 ms	100–800 ms	100–800 ms
Frequency	1 MHz	1 MHz	460 KHz	2 MHz	Unknown	1 MHz	2 MHz
Multiple pulses	No	Yes	No	No	No	No	No
Monopolar RF	Yes	No	No	No	Yes	No	No
Bipolar RF	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Impedance Monitor	Yes	No	Yes	No	No	No	No
Needle Count	49	12, 24, 40	8, 14, 49	64, 25, 10, 6	1, 16, 25, 49	36	25
Needle Depth (mm)	0.50–2.0	0.5–7.0	0.1–3.5	0.50–3.5	0.50–2.0	0.50–3.5	0.50–3.5
Control Depth	0.5, 0.8, 1.5, 2.0 mm	0.1 Step	0.1 Step	0.1 Step	0.1 Step	0.1 Step	0.1 Step
Allowed Shot Count	2,000	Unknown	Unknown	Unknown	1,000	Unlimited	N/A

Hz, hertz; KHz, kilohertz; MHz, megahertz; mJ, millijoule; mm, millimeter; ms, millisecond; N/A, not applicable; pps, pulse per second; RF, radiofrequency; V, volt; W, watt.

and duration settings with needle-based fractional RF for rhytids and skin laxity at 67°C and 3 seconds.[15] Lower target temperatures yielded less denatured collagen and, thus, suboptimal results. Although some report that skin of colour requires lower target temperatures to prevent dyspigmentation, Teymour et al. discuss that RFMN is preferred over lasers due to its ability to target specific thermal zones and depths and, thus, minimal risk of dyspigmentation.[16] Still, insulated probe tips may help prevent dyspigmentation in skin of colour patients.

Broadband infrared light

Some of the original devices employ broadband infrared light (1,100–1,800 nm), specifically targeting water as its chromophore, thereby inducing collagen denaturation. This denaturation process subsequently triggers collagen remodelling and organisation, tightening tissue. Several popular devices have emerged within this category, including Titan® by Cutera, StarLux IR™ by Palomar Medical Technologies (now Cynosure), SkinTyte® by Sciton, and Tripollar™ by Pollogen. Several of these devices are equipped with cooling mechanisms to enhance patient comfort during treatment. For skin of colour patients, higher filters are less likely to lead to pigmentation. However, more treatments may be necessary to achieve the desired outcome.[9]

High-intensity focused ultrasound and micro-focused ultrasound

Though originally used to treat cancerous and noncancerous tumours, high-intensity focused ultrasound (HIFU) entered the aesthetic arena for lipolysis and skin tightening. HIFU uses non-ionizing ultrasound waves to 1) induce thermal injury at the dermal layer to cause necrosis of dermal adipocytes and subsequent collagen fibre retraction and 2) create cavitations at the subcutaneous layer, leading to coagulation and apoptosis of adipocytes.[17] Ultrasound therapy does not target melanin because melanin is not a chromophore at that wavelength. Thus, patients with darker skin types have a much lower risk of pigmentation sequelae when compared with other techniques such as laser or RF.[9,18]

From the existence of HIFU, a subclassification called micro-focused ultrasound (MFU) was born. Unlike HIFU, which utilises thermal and cavitation effects, MFU only uses the thermal effects due to its high frequency and short pulse duration. MFU technology thermally ablates a small area (<1 mm3) of the dermis, leaving a small surrounding area of undamaged tissue. The array of thermal injury zones alternating with untreated skin allows for the bridging of undamaged tissue and promotes rapid healing. Ulthera® by Merz Aesthetics is a popular MFU device that is approved by the FDA for lifting the eyebrow, submental, and neck, as well as tightening the skin of the décolleté. Ulthera® is particularly unique due to its use of real-time ultrasound imaging during the procedure, so the user may precisely deliver energy to the target tissue depth. A prospective multicentre pilot study tested MFU safety and efficacy for the décolleté in which clinicians blindly assessed aesthetic improvement at 90- and 180-days post-treatment. In the blind clinical assessment, 66.4% of patients showed "improvement" or "much improvement" at 180 days, 82.7% of patients subjectively reported noticed improvement; however, 41% of patients in total were "neither satisfied nor dissatisfied," "dissatisfied," or "very dissatisfied."[19]

HIFU/MFU devices have several interchangeable hand pieces, each providing varying focus depths and/or frequencies. The depth needed for proper treatment at the level of the dermis or sub-dermis may vary depending on the patient's body habitus or desired outcome. Frequency and tissue depth penetrance are indirectly related; lower frequency transducers can provide deeper treatment depth. Focus depth and skin depth are directly related; the 1.5 mm and 3 mm handpieces are best suited for the reticular dermis (periorbital and perioral regions), whereas the 4.0 mm and 4.5 mm hand pieces target the deeper sub-dermal tissues (jawline and brow regions).

Synchronous ultrasound parallel beam

Synchronous ultrasound parallel beam (SUPERB) generates high-intensity, high-frequency waves that exclusively target the mid-dermal layer (depth of about 1.5 mm). The single handpiece comprises seven transducers and, thus, creates seven cylindrical thermal zones in the dermis that are arrayed parallel to the collagen fibres. This thermal event partially denatures collagen and elastin to stimulate their remodelling. The handpiece also has a sophisticated cooling system that provides real-time skin temperature feedback to protect the epidermal layer. Sofwave™ by Medical Ltd has FDA clearance for facial fine lines and lifting the brow, submentum, and neck regions. Most recently, Sofwave™ was cleared for the treatment of lower body cellulite. Sofwave™ is often compared to Ulthera® due to their similarities in ultrasound technology (**Table 2**).[18] Because SUPERB is a newer device to the market, efficacy data from trials are limited. One study of 36 Thai participants (Fitzpatrick skin type II–IV) showed improvement in mean depression volume in the nasolabial folds and marionette lines at 1 and 3 months. Patient satisfaction was not reported. Adverse effects, such as skin blistering and hyperpigmentation, were not observed.[20] Similar to HIFU and MFU modalities using ultrasound energy, SUPERB should be safe for skin of colour, though data remains limited.

Table 2. *Comparison of Sofwave (SUPERB technology) and Ulthera (HIFU technology) characteristics.*

Characteristic	SUPERB (Sofwave™)	HIFU/MFU (Ulthera®)
Mechanism of stimulating collagen	Thermal effect via seven cylindrical thermal zones within one depth of dermis	Thermal effect via ultrasound energy at varied depths of dermis
Number of unique hand pieces	Only 1	Interchangeable, up to 4
Pulse amount	7–8x	1x
Real-time ultrasound imaging	No	Yes
Target tissue depth	Superficial (1.5–2 mm)	Varied (1.5–4.5 mm)
Treatment time	Shorter: 30–45 minutes for full face and neck	Longer: 30–60 minutes for face; 30–45 minutes for neck
Pain tolerance	Slightly less painful due to shallower depth of treatment	Slightly more painful due to deeper depth of treatment

HIFU, high-intensity focused ultrasound; MFU, micro-focused ultrasound; mm, millimeter; SUPERB, synchronous ultrasound parallel beam.

Rapid acoustic pulse™ technology

Rapid Acoustic Pulse™ (RAP) technology represents an innovative approach to addressing skin laxity. This non-invasive treatment option utilises acoustic waves to achieve long-term improvements. Notably, RAP stimulates the production of new collagen III and elastin within the dermis even after a single session.[21] RAP harnesses acoustic waves and enhances microcirculation, lymphatic drainage, and nucleogenesis. RESONIC™ by Allergan is FDA-approved for cellulite treatment and stands out as the first in its class.

Dermal micro-coring® technology

Dermal micro-coring® technology (MCT), known as Ellacor® by Cytrellis Biosystems, is a novel technology that is FDA-approved to address moderate-to-severe skin laxity by removing excess skin. Ellacor® is indicated for skin laxity of the mid and lower face, though other studies have also tested its efficacy in abdominal skin tightening. Micro-coring uses hollow, hypodermic needles with diameters <0.5 mm (and thus below the threshold of scarring) to remove micro-cores of skin. MCT is considered superior to RF due to the more immediate skin closure along relaxed skin tension lines without thermal energy. Clinical trials have shown biopsy-proven histologic absence of scarring without significant difference in erythema index nor melanin index. In addition, trials have shown increased skin thickness, decreased skin surface area, and global aesthetic improvement on the facial skin.[22]

Electromagnetic energy

Though electromagnetic energy does not stimulate neocollagenesis, it is often used in conjunction with the modalities reviewed in this chapter to provide a holistic approach to skin tightening. Because these modalities do not employ heat or light, electromagnetic energy can be used safely on skin of colour.

High-intensity focused electromagnetic field

The mechanism for high-intensity focused electromagnetic field (HIFEM) is not fully understood; however, studies have shown that magnetic resonance may improve muscle thickness, strength, and tone. A possible mechanism of skin tightening is that the rapid muscle contractions caused by HIFEM initiate three phenomena that work synergistically: apoptosis of fat cells, muscle hypertrophy, and decreased distance between large abdominal muscles. HIFEM may also allow for minimal fat loss. Others propose that the adipose tissue is compressed by surrounding hypertrophied muscle, allowing for a smoother appearance on the surface of the skin and creating a more aesthetic result in the target area. Emsculpt® and Emsculpt NEO® by BTL Industries use HIFEM or a combination of HIFEM and RF to increase muscle tone and contour the body.[23]

Magnetic muscle stimulation

Magnetic muscle stimulation (MMS) uses electromagnetic energy to generate a current that allows for depolarisation and, thus, initiation of an action potential in muscle fibres. The electrically stimulated muscle contractions mimic high-powered

strength exercises to target muscle tissue. CoolTone™ by Allergan is an FDA-approved device that strengthens targeted muscles in the abdominals, thighs, and buttocks to provide a more sculpted appearance in the region treated. The non-invasive procedure is generally well-tolerated and has high satisfaction rates among patients. The patient's BMI should be considered when assessing a patient's candidacy for MMS treatments. Patients with lower BMI may notice results sooner than those with higher BMIs. One study observed the greatest difference from baseline was in participants with a BMI range of 25–30.[19] MMS is unique in that it targets muscle rather than collagen for tightening and toning. Because participants see muscle tone in a relatively short amount of time, the authors have subjectively observed patients stating that the quick results and new strength have motivated them to exercise more to maintain their results. The secondary health benefits from MMS treatments have not been heavily explored, though patients' increased motivation is a testament to how treating skin laxity may improve patients' self-confidence.

Looking ahead: Elastogenesis

An emerging area of research is in elastin regeneration. Elastin is an extracellular matrix protein that functions to maintain skin elasticity, structure, durability, and, consequently, one's youthful appearance. As the skin ages and is exposed to harmful environmental factors, elastic fibres become damaged and disorganised. Patients with solar elastosis or chronically sun-damaged skin have a disrupted elastin fibre network.[24] The disorganised elastin network allows for skin laxity, fragility, and uneven texture. Native elastin exhibits a remarkably low turnover rate, making it challenging to undergo repair or replacement once damaged. Currently, no established treatments stimulate elastogenesis, as the process of generating new elastin is considerably more intricate than that for collagen. Even more difficult, as biologically, elastin production ceases in early adulthood.[25] However, clinical trials are on the horizon. Allergan has initiated clinical trials to assess whether a delivery vehicle of tropoelastin can replenish elastic fibres. Until then, current treatments, such as sunscreen and antioxidants, remain the standard of care for preserving elastin.[24]

Conclusion

The mechanism of neocollagenesis has been applied to many cutting-edge devices to combat skin laxity. Major limitations to understanding the efficacies of treatment devices exist: most devices lack comprehensive, large-scale randomised clinical trials, as this is not required for FDA approval. In addition, many of the published trials lack diversity in skin types. Practitioners must set realistic expectations for patients in their treatment of choice for skin laxity. Though this review discusses non- and minimally invasive procedures, surgical intervention should be considered in cases of severe laxity. Different devices on various skin types may render certain side effects and outcome profiles; RFMN is a safe device for skin of colour. Targeting elastin production remains an avenue of investigation for addressing skin laxity.

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Q&A

What are your favourite cosmeceutical ingredients?

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Retinoids have been at the core of dermatologist-recommended skincare for many years, with both cosmetic and therapeutic benefits. These analogues of Vitamin A, of which the active metabolite is retinoic acid, penetrate the epidermis and superficial dermis to exert numerous functions, including regulating cell apoptosis, differentiation, and proliferation. An all-rounder in the dermatologist's armamentarium, applications include the treatment of acne, pigmentation, photodamage, superficial rhytids, numerous inflammatory dermatoses, ichthyoses, and hyperkeratotic disorders.

They can also serve an adjunctive role in skin preparation to enhance outcomes of other topical or physical treatments, such as 5-FU or photodynamic therapy (conventional or laser-assisted).

Specific cosmetic benefits include increased keratinocyte proliferation, strengthening of the epidermis, increased collagen, and reduced transepidermal water loss (TEWL), ultimately leading to improved skin texture, tone and luminosity. However, it takes commitment and time (I find >6 months) for our patients to reach such visible benefits.

There is a well-established side effect profile, such as irritation and sun sensitivity. Still, with adequate education and persistence, tolerance can build – much like fitness when training for a marathon.

Having said that, I don't believe every patient should be prescribed our maximum strength formulation, a trap we occasionally fall into.

There is a wide range of retinoids available in both the pharmaceutical and cosmeceutical spaces (including the more recent attention on hydroxypinacolone retinoate [HPR]), and variation in formulation, stability and additional ingredients will determine what is most appropriate for an individual patient, including lifestyle, skin concerns, medical history, and of course, affordability.

Whilst it's an exciting era to witness rapid scientific advances producing new actives on our horizon, I'd be remiss to exclude our sometimes unacknowledged but, in my opinion, very deserving workhorses – the skin acids. I'm being greedy to use this umbrella term. If my hand were forced, I'd say the alpha hydroxy acids (AHAs), generally at 5–10% in over-the-counter products, are still among my favourite cosmeceuticals for skin texture, luminosity and glow, with actions against pigment, acne, and appearances of ageing. These hydrophilic chemical exfoliants exist in various formulations, including cleansers, serums, creams/lotions, and peels appropriate for dry and sensitive skin, or equally pack a powerful punch depending on treatment goals and irritation threshold. Glycolic acid, the smallest molecule of them all, thus possessing the greatest rate and depth of skin penetration, exfoliates while boosting hydration and collagen production, hence an excellent option to incorporate into a regime of patients with signs of ageing and photodamage, with decent resilience/tolerance. Lactic acid, derived from sour milk (used by the Ancient Egyptians to improve skin appearance), is slightly gentler and a valuable option for pigmentation, often in conjunction with other products and treatments, including as a skin preparatory adjunct before other topical or physical therapies. Finally, I think mandelic acid, the largest AHA molecule, is a dark horse that deserves some recognition. It is slower and gentler but capable of tackling ageing and pigmentation and gaining the desired radiant glow characteristic of the AHAs. In my experience, it is an excellent option for sensitive skin, including rosacea.

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Any dermatologist will say that their favourite skincare product is sunscreen. I will take it one step further and say that zinc oxide is one of my favourite skincare ingredients. We all know about its effectiveness as a physical blocker in sunscreen – it is broad-spectrum, blocking both UVA and UVB rays, but is also photostable and water resistant. There is less potential for irritation as it sits on the surface of the skin, making it a good choice for those with sensitive skin. In addition to its UV-blocking properties, zinc oxide is anti-inflammatory, a potent antioxidant, non-comedogenic, and inhibits excessive oil production. So, it is an excellent choice for those with oily and acne-prone skin. In lower concentrations in cosmeceuticals, it can be used to treat inflammatory dermatoses, including rosacea, atopic dermatitis, and psoriasis. Historically, one of the biggest complaints about zinc oxide is its chalkier consistency and propensity to leave a white cast on the skin. However, this is less of an issue with evolving modern formulations. A recent social media trend has been to use zinc oxide to "baste" the skin. This moisturising technique involves applying a layer of cream with a high percentage of zinc oxide as your last skin-care step before bed, with the idea that you will wake up with hydrated and smooth skin in the morning. Whilst I have never recommended this to my patients, the La Roche Posay Cicaplast Baume and the Avene Cicalfate also contain zinc oxide as well as other nourishing ingredients, so if the skin is irritated, then I think these are an excellent alternative to "basting" with nappy rash cream!

Another favourite cosmeceutical ingredient of mine is niacinamide, which is increasingly found in many products. Niacinamide is a small-molecule hydrosoluble vitamin with essential metabolic functions in mammalian cells. It plays a pivotal role in NAD+ synthesis by contributing to redox reactions and energy production in cutaneous cells. It is also known to influence human DNA repair and cellular stress response. Therapeutically, it is effective in managing acne vulgaris, melasma and psoriasis; from a cosmeceutical perspective, it has been used as a multipurpose anti-ageing ingredient, having been shown to reduce cutaneous oxidative stress, inflammation, and pigmentation significantly. Being anti-inflammatory and restoring the skin barrier, it is safe and effective in all skin types, and I do not hesitate to recommend it to most of my patients. My preferred way to use it is in a serum applied to clean skin in the morning, followed by a moisturiser and sunscreen. I have found 10% to be sufficient. This is an excellent substitute for those who do not tolerate vitamin C.

In dermatology, where efficacy and safety intertwine with patient satisfaction, hydroquinone stands out as an effective cosmeceutical for melasma, supported by clinical trial data. In my practice, it is also commonly prescribed four weeks before and after pigmentation laser therapy to enhance results and minimise complications. Patients are advised to stop using it 1–2 days pre- and post-laser to prevent local irritation, although this is not a contraindication for the procedure. The primary concern with hydroquinone is irritant dermatitis, making it crucial to find the right concentration—4% is the most widely accepted strength for treating melasma. The traditional three-month limit for use can be restrictive due to the inevitable rebound of melasma; I recommend a regimen of three months on, followed by one month off, allowing patients who do well to gradually extend the "off period" if there's no sign of rebound. During treatment, patients should avoid irritating ingredients and foamy cleansers. I often suggest a "short contact" routine, where they wash the product off after 10–15 minutes or 5 minutes for sensitive skin. While overnight use may yield faster results, it can sometimes lead to undesirable hypopigmentation, which is usually reversible with short-term use. Regular reviews every 12 months are essential to monitor for irritation, atrophy (from the accompanying topical steroid), bleaching effects, and ochronosis and to adjust concentration as needed. Over-the-counter 2% hydroquinone is available for mild cases of melasma, but many patients with melasma will struggle to find that this leads to satisfactory improvement.

Another favourite of mine is peptide serum. Peptides, as short-chain amino acids, play various roles in skin health, serving as building blocks for skin structure, enhancing signals for elastin and collagen production, facilitating the absorption of trace elements for wound healing, and inhibiting matrix metalloproteinases to prevent dermal breakdown. Peptide serums are well-tolerated and lack irritant effects, making them excellent complements to more irritating agents like retinol or ascorbic acid. Over the years, I have observed a rise in patients, especially in the Asian population, presenting with rosacea or sensitive skin due to unsuitable skincare routines or excessive skin therapies. In these patients who seek anti-inflammatory and anti-ageing cosmeceuticals, I often recommend niacinamide followed by peptides, as options are limited. However, the main drawbacks of peptides are their relatively high cost and uncertainty regarding their penetration depth into the dermis. Nevertheless, promising *in vitro* evidence supports their efficacy, which I hope will translate to real-world benefits.

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