Review article / Artykuł przeglądowy

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Investigation of the anti-inflammatory and antioxidant properties of cannabis in cosmeceuticals

Badanie właściwości przeciwzapalnych i przeciwutleniających konopi indyjskich w kosmeceutykach

ABSTRACT

Biotechnology, as an interdisciplinary scientific field, is crucial in identifying the valuable active ingredients of plants. Their application extends beyond medical and pharmaceutical formulations to encompass cosmetics, in which these natural substances play a significant role.

This article aimed to investigate the potential advantages of integrating cannabis-derived compounds into skincare cosmetic formulations. Their therapeutic efficacy on diverse dermatoses was emphasised. The diverse applications of cannabinoids and terpenes in cosmetic formulations were also examined.

Scientific report analysis confirms the beneficial effects of cannabis-derived compounds, including cannabidiol and seed oil, in enhancing skin health and addressing inflammation and dermatological issues. The potential of cannabis-derived compounds in creating novel and effective cosmeceutical products was emphasised.

Keywords: cannabinoid, anti-inflammatory effects, cosmeceutical, cannabis, antioxidants

STRESZCZENIE

Biotechnologia, jako interdyscyplinarna dziedzina nauki, odgrywa ważną rolę w odkrywaniu cennych składników aktywnych roślin. Ich zastosowanie wykracza poza preparaty medyczne i farmaceutyczne, obejmując także kosmetyki, w których te naturalne substancje pełnią istotną rolę.

Celem artykułu było zbadanie potencjalnych korzyści z włączenia związków pochodzących z konopi indyjskich do preparatów kosmetycznych pielęgnujących skórę. Podkreślono ich terapeutyczny wpływ na różnego rodzaju dermatozy. Omówiono również różnorodne zastosowania kannabinoidów i terpenów w produktach kosmetycznych.

Analiza doniesień naukowych potwierdza pozytywny wpływ składników pochodzących z konopi indyjskich, takich jak kannabidiol oraz olej z nasion w promowaniu zdrowia skóry, terapii stanów zapalnych oraz problemów dermatologicznych. Podkreśla się obiecującą rolę związków pochodzących z konopi indyjskich w opracowaniu innowacyjnych i skutecznych produktów kosmeceutycznych.

Słowa kluczowe: kannabinoid, działanie przeciwzapalne, kosmeceutyk, konopie indyjskie, przeciwutleniacze

INTRODUCTION

Since ancient times, people have utilized the herbaceous plant *Cannabis sativa L.* (*Cannabaceae*) for food, fibre, oil, and medicinal purposes. When Emperor Chen Nung, the founder of Chinese agriculture, created the country's first pharmacopoeia, he suggested using cannabis seeds to treat inflammatory illnesses like psoriasis and dermatitis. This signified the beginning of recognition of cannabis in therapeutic application. Besides its topical application in Indian traditional medicine, cannabis was utilised for the treatment of eczema and pruritus in Western Europe and America during the late 19th and early 20th centuries [1, 2].

Around 500 components are found in plants of the genus Cannabis. 125 of these are known to be cannabinoid-type chemicals, while the other constituents are categorized into non-cannabinoid types such as flavonoids, alkaloids, non-cannabinoid phenols, as well as terpenes [2]. Additionally, various parts of the cannabis plant and their respective locations contain differing concentrations of medicinal secondary compounds [3]. Due to differences in the content of active substances, extracts from cannabis flowers and seeds can differ substantially from each other [4]. As a result, there are distinctions between extracts from various portions of the plant. Understanding the discrepancy among various sections of the cannabis plant is essential for investigating their potential applications and effects. The three types of cannabinoids are derived from plants and are found in higher concentrations in flowers. These include phytocannabinoids, that are derived from tetrahydrocannabinol (THC) alongside cannabidiol (CBD) and endocannabinoids, which are generated through metabolism in the human body [5].

Research on the human endocannabinoid system (ECS) has led to an exploration of novel and targeted treatments using drugs derived from cannabis. It is becoming more and more clear that aiming ECS can result in the development of innovative and intelligent drug delivery technologies [6]. According to Sheriff et al. (2020), the skin possesses a functional ECS with cannabinoid receptors in keratinocytes, glands that produce sebum, hair follicle cells, perspiration gland cells, neurons for sensation, immune system cells, mast cells, and fibroblasts. Skin problems including acne, psoriasis, seborrheic dermatitis, allergic contact dermatitis and even skin cancer may be related to disruption of the epidermal growth layer. Certain skin problems have been suggested to be treated by specialized agonists as well as inhibitors of the receptors for cannabinoids (CB1 and CB2). These drugs work by activating or inactivating these receptors [7].

This article offers a description of various CBD-infused skincare products currently available, alongside an overview of recent studies regarding the topical application of CBD and the associated risks stemming from its chemical structure that render it hazardous for such use. Various methods and formulations have been examined to enhance the efficacy of CBD.

CANNABINOIDS IN SKINCARE

Tetrahydrocannabinol

THC, or delta-9-tetrahydrocannabinol, is the most thoroughly researched substance. The intoxicating effects that come

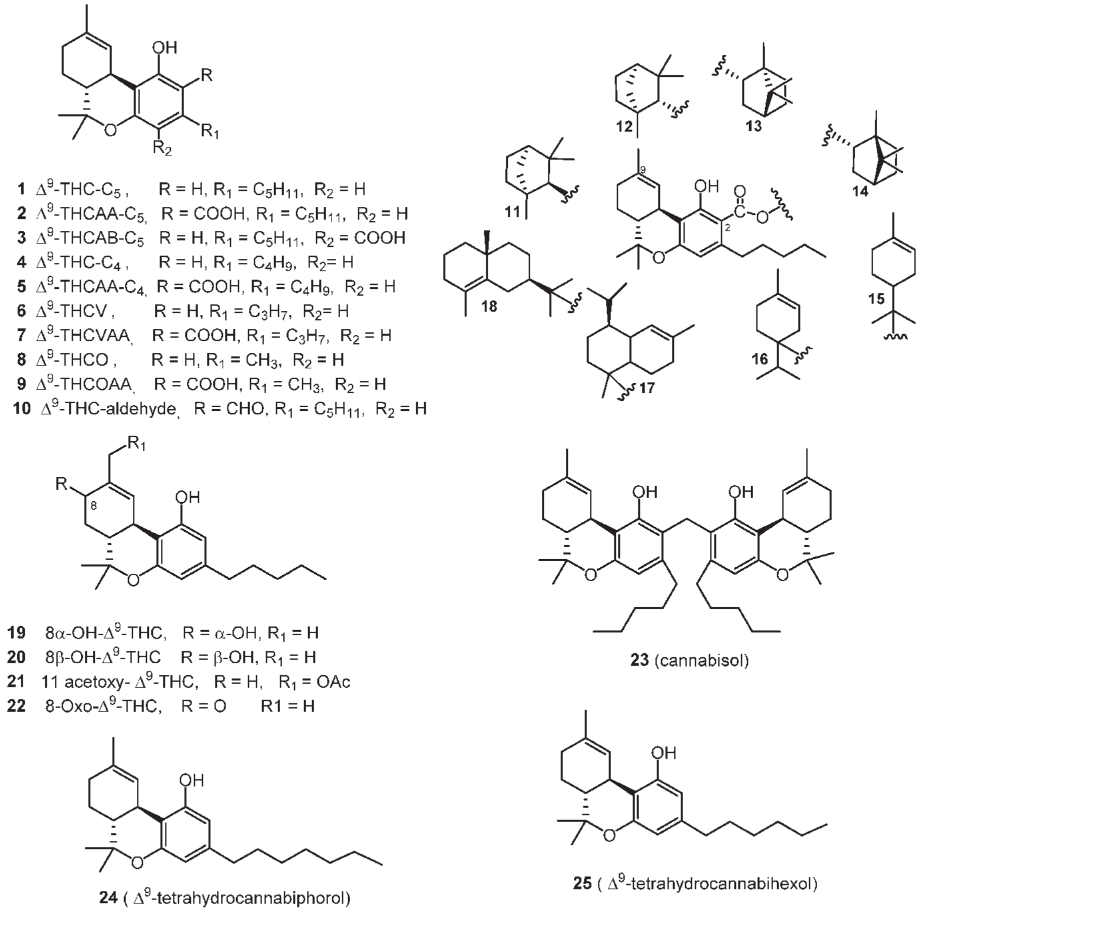
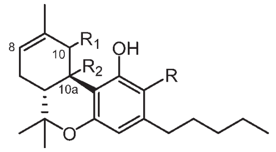


Fig. 1 Structure of THC-type cannabinoids **Source:** [8]



26 Δ^8-THC, R = H, R_1 = H, R_2 = H
27 Δ^8-THCA, R = COOH, R_1 = H, R_2 = H
28 10α-OH-Δ^8-THC R = H, R_1 = α-OH, R_2 = H
29 10β-OH-Δ^8-THC R = H, R_1 = β-OH, R_2 = H
30 10aα-10-oxo-OH-Δ^8-THC, R = H, R_1 = O, R_2 = OH

Fig. 2 Structure of Δ^8-THC-type cannabinoids **Source:** [8]

with consuming cannabis are caused by THC. Due to its psychoactive qualities, cannabis was historically mostly used for recreational purposes [8, 9]. Recently, there has been significant interest in its potential medical applications. The U.S. Food and Drug Administration (FDA) acknowledges the potential benefits of cannabis for medicinal uses as well as the need for further research to prevent unanticipated adverse effects [10]. Goani and Mecholum (1964) reported isolating purified (–)-Δ9-trans-tetrahydrocannabinol (Δ9-THC, 1) from a cannabis hexane extract by column chromatography over florisil and then alumina. A crystalline derivative of THC was developed called nitrophenylurethane, and then further purified it using moderate alkaline hydrolysis. Its chemical structure was clarified by infrared (IR) and nuclear magnetic resonance (NMR) spectroscopy methods. Using a cellulose powder column eluted with a hexane and dimethylformamide combination, preparative thin-layer chromatography was used in 1967 to isolate (–)-Δ9-trans-tetrahydrocannabinolic acid A (Δ9-THCAA, 2). A combined approach of ultraviolet (UV), IR, and NMR spectroscopy research was used to determine the molecular structure of THCAA [8-11]. Fig. 1 presents the various structures of THC-Type Cannabinoids.

In 1966, cannabinoids, specifically (–)-Δ8-trans-tetrahydrocannabinol (Δ8-THC), were isolated from the leaves and flowers of cannabis plants grown in Maryland. By using benzene as an eluent in silicic acid column chromatography, Δ8-THC was isolated from the petrol-ether extract. Nine years later, the methyl ester of its carboxylic acid, Δ8-trans-tetrahydrocannabinolic acid A, (fig. 2) was extracted from a cannabis plant that originated in Czechoslovakia.

CANNABIGEROL AND CANNABIDIOL

The atomic structure of (E)-CBG (31) was verified by synthesis, after cannabigerol (CBG) was extracted from cannabis resin in 1964 using florisil chromatography. It was established in 1975 that cannabigerolic acid (CBGA) was the first cannabinoid produced in the Δ9-THCAA biosynthesis pathway when CBGA as well as the monomethyl ether of CBGAA were isolated. By heating the hemp extract with toluene for seven hours, and purification using column-based chromatography (silica-gel column) using benzene as the eluent, the monomethyl ether of (E)-CBG was recovered from the hemp extract in benzene [8-10]. A lot of research has been conducted in the past few years on the therapeutic benefits of cannabis and related compounds. The ECS has previously been identified in the skin, and while there is still much to learn about its role and significance in maintaining skin homeostasis, it is becoming ever more integral to a promising future in the treatment of dermatological disorders [12]. The primary non-intoxicating phytocannabinoid in cannabis, CBD, has been found to have anti-inflammatory, antioxidant, wound-healing, sebostatic, anti-pruritic, antimicrobial, and photoprotective properties in addition to regulating hair growth [13]. Fig. 3 presents all of the cannabinoids of the CBG type. In 2020, cannabitwinol, a CBD dimer derived from hemp hexane extract, was isolated and identified. A combination of ACN/H_2O/formic acid (7:3:0.1) was used as the mobile phase for the chromatography of the hexane extract on a silica column, which was then eluted with hexane/CH_2Cl_2. This was followed by semi-preparative high-performance liquid chromatography C18-HPLC. Extensive 1D along with 2D NMR at −30°C was used to identify the chemical structure of CBDD, and HRESIMS as well as tandem mass (MS/MS) spectrometry were used to confirm it. The decarboxylated ethanol solution of hemp leaves were separated from cannabidiol monomethylether using florisil as well as silica gel chromatography in a column [12, 13].

As a result, CBD has received significant attention for its potential efficacy in addressing cutaneous pathologies like atopic dermatitis, psoriasis, acne, epidermolysis bullosa, systemic sclerosis, seborrheic dermatitis, androgenetic alopecia, even though there is currently a lack of scientific evidence supporting its bioactivities and that some of its mechanisms of action are still elusive [15, 16]. The physicochemical properties limit topical administration, requiring the development of innovative technological methods to penetrate the skin's intact barrier [17]. As of now, the precise mode of action of CBD is not entirely understood. CBD is known to act on cannabinoid receptors of the ECS and is found across the body, including the peripheral and central nervous system, as well as the brain [18]. Many physiological reactions of the body, such as pain, memory, appetite, and mood, are regulated by the ECS. More precisely, CB1 receptors are located in the brain and spinal cord's pain pathways, where they may influence the analgesia and anxiety caused by CBD, whereas CB2 receptors are situated on immune cells, and they may affect the anti-inflammatory processes induced by CBD [19, 20]. Fig. 4 displays all of the cannabinoids of the CBD type.

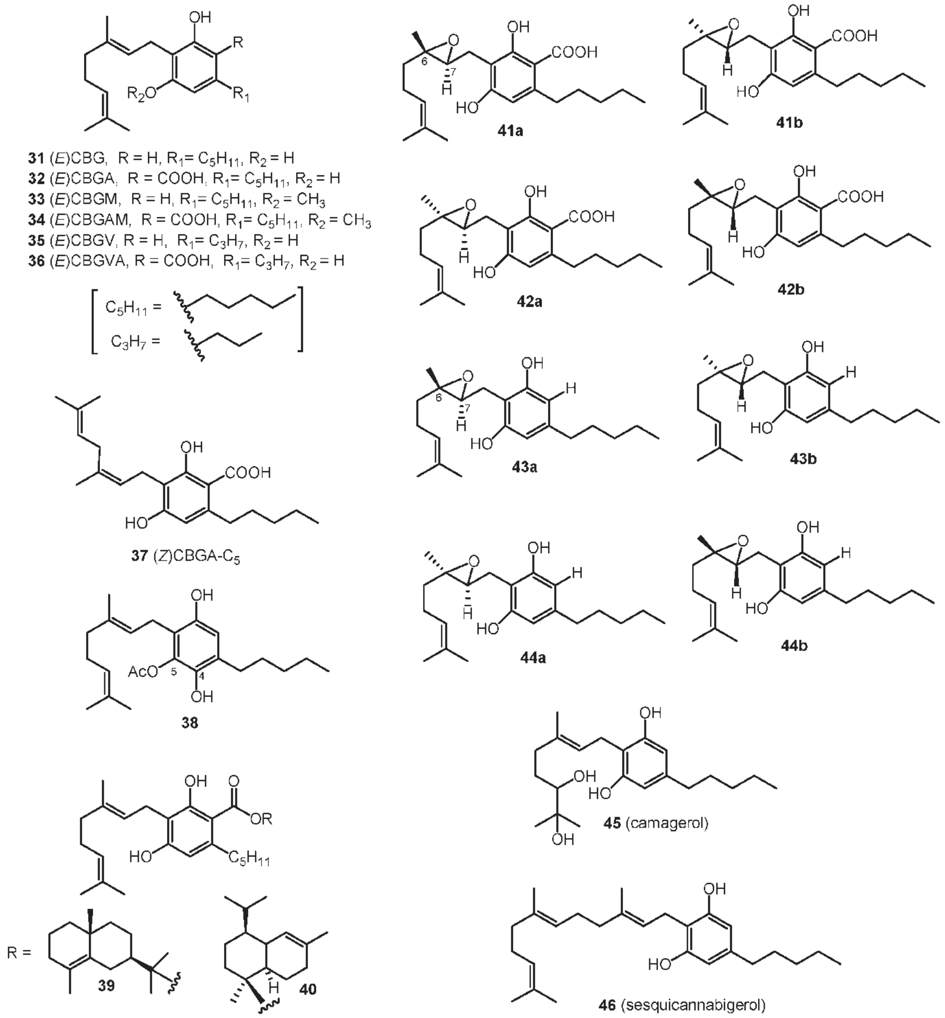


Fig. 3 CBG-type cannabinoids **Source:** [14]

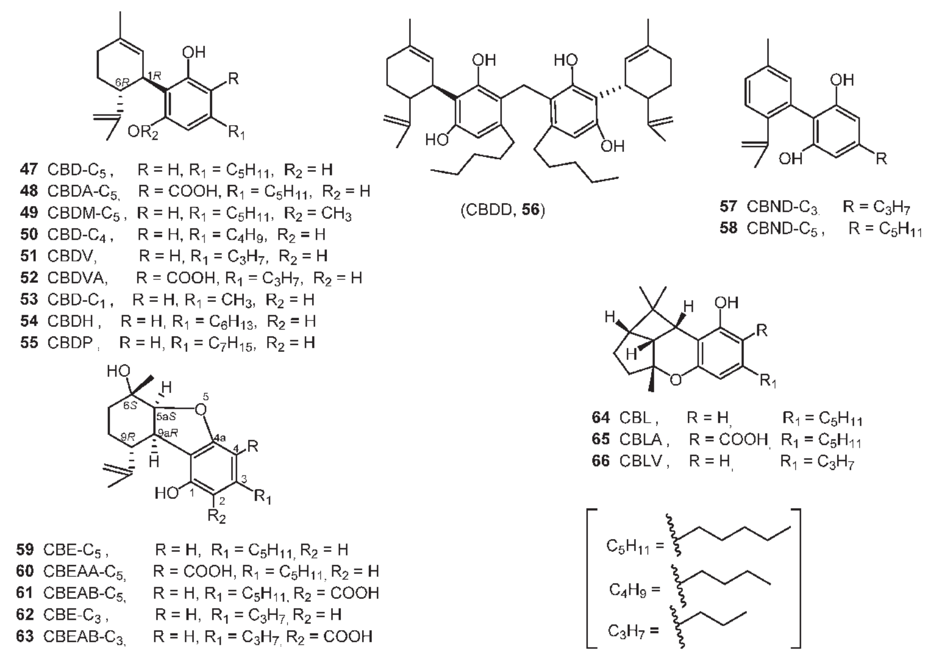


Fig. 4 CBD, CBND, CBE and CBL-type cannabinoids **Source:** [8]

TERPENES

Terpenes are a diverse array of organic compounds present in numerous plants, including cannabis, fruits, and herbs. They significantly augment the flavour and aroma of these plants, and the beauty industry is keen on utilising them for their potential health benefits [21]. Terpenes have several benefits for skincare, including aromatherapy, anti-inflammatory, antioxidant, hydrating and moisturizing properties, antibacterial and antifungal activities, and increased product performance [22]. While terpenes in skincare products may offer advantages, maintaining caution in their application is essential. Prior to applying products to extensive skin areas, patch testing is generally recommended, as certain people may exhibit allergies or sensitivities to specific terpenes [23]. Furthermore, to ensure both safety and efficacy, the concentration and formulation of terpenes in skincare products should be carefully considered.

Terpenes, which are found in many plants, can benefit skin health by having anti-inflammatory, antioxidant, and antimicrobial properties [16].

- Anti-Inflammatory properties. Numerous terpenes have shown anti-inflammatory potentials, including limonene, beta-caryophyllene, and alpha-bisabolol [24]. Chronic inflammation is a common feature of various dermatological conditions, including psoriasis, eczema, and acne [25]. Topical application of these terpenes may alleviate skin redness, swelling, and irritation, promoting a more tranquil and balanced complexion [21].
- Antioxidant effects. Terpenes with antioxidant properties include pinene, limonene, and myrcene. Antioxidants protect the skin from free radical-induced oxidative damage such as fine wrinkles, and early ageing [26].
- Moisturising and hydrating. Essential oils frequently contain terpenes like linalool and geraniol, which help skincare products retain their moisture and hydration. They also keep the skin hydrated [27]. Terpenes can have a calming and soothing effect on the skin. For example, linalool, which has calming potential, is frequently found in skin care products intended for sensitive or irritated skin [30]. These terpenes can lessen skin irritation-related redness and discomfort.
- Antibacterial and antifungal properties. Research has demonstrated the antibacterial and antifungal properties of terpenes, including pinene and terpinolene [21]. This renders them advantageous in skincare formulations designed to address bacterial or fungal infections and various dermatological conditions including acne.
- Product efficacy. Terpenes can act as penetration enhancers, assisting other active ingredients in skincare products to penetrate the skin more effectively. This means that terpene-containing products can deliver their benefits more efficiently, increasing the product's overall efficacy [22].
- Aromatherapy benefits. Aromatherapy benefits can be obtained by inhaling the aroma of terpenes found in skincare products. Scents like lavender (with linalool), for example, have a calming effect, reducing stress and promoting relaxation.

Fig. 5 illustrates the production process for terpenes from *Cannabis sativa*. While terpenes may have potential benefits for skin health, individual sensitivities and allergies may vary. Before using terpene-containing skincare products, it is

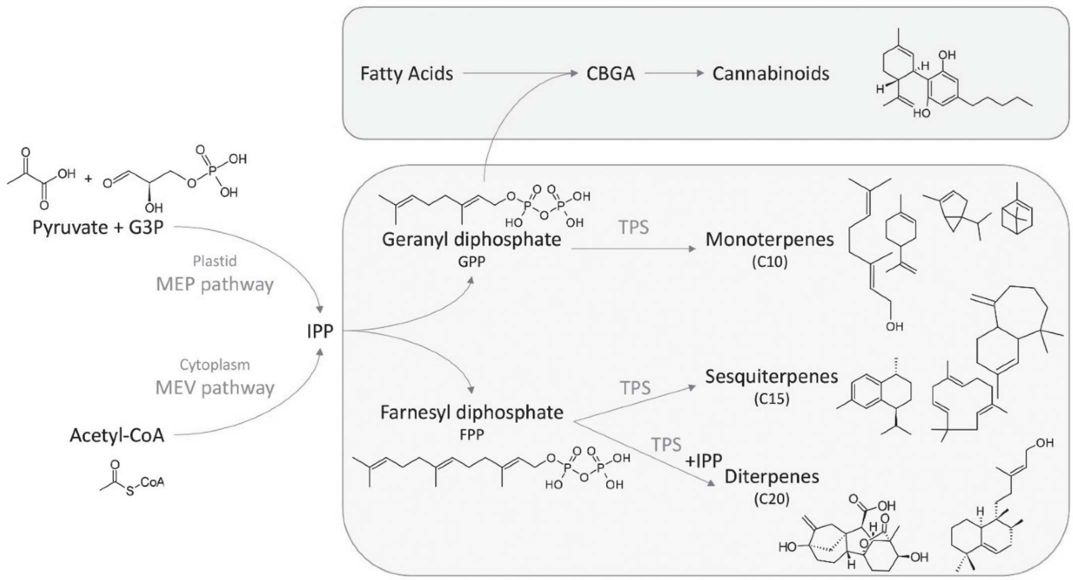


Fig. 5 An overview of the *Cannabis sativa* terpenes production process **Source:** [29]

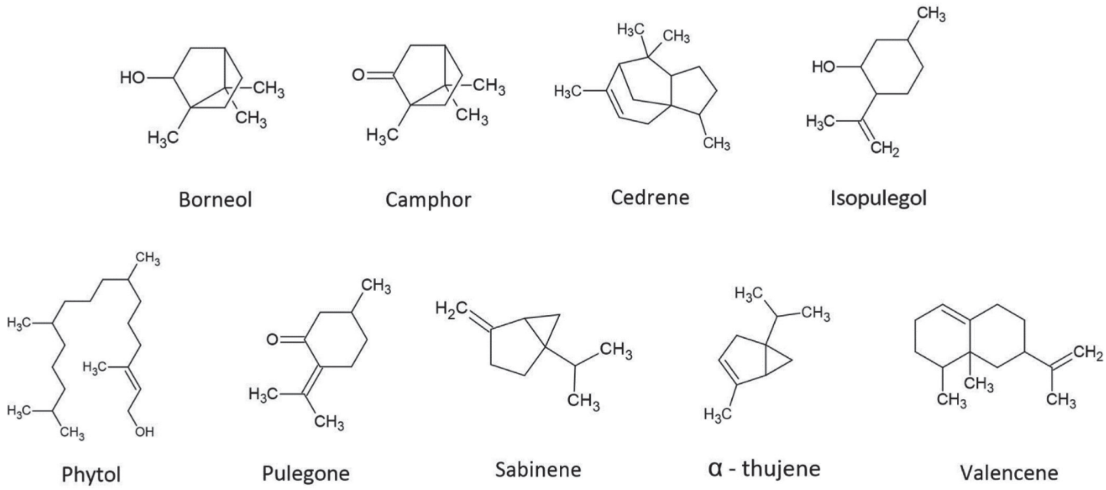


Fig. 6 Structure of various types of terpenes derived from cannabis **Source:** [28]

advised to perform a patch test to ensure that the skin does not react negatively. Additionally, the concentration of terpenes in products and their overall formulation should be carefully considered to confirm safety and effectiveness.

Fig. 6 presents the structures of various terpenes.

ANTI-INFLAMMATORY AND ANTIOXIDANT PROPERTIES

Cannabinoids as modulators of inflammation

The literature on cannabinoids as modulators of inflammation is extensive and compelling. CB and THC are among the prominent cannabinoids studied for their anti-inflammatory properties. CBD, in particular, has shown promise in suppressing inflammatory responses through various mechanisms, such as inhibition of pro-inflammatory cytokines [30]. THC, while having anti-inflammatory effects, can also exhibit immunomodulatory actions. The interaction of cannabinoids with the ECS plays a crucial role in regulating inflammation, making them potential candidates for therapeutic interventions in inflammatory conditions [31].

- Pro-inflammatory cytokine inhibition. Inflammatory mediators are responsible for orchestrating the process of inflammation. When an infection occurs, active macrophages release pro-inflammatory cytokines including interleukin-1β (IL-1β) and tumour necrosis factor alpha (TNF-α). TNF-α and IL-1β function by binding to certain receptors on cell membranes, which aid in attracting and triggering polymorphonuclear neutrophils at the infection site. Developing transforming growth factor beta (TGF-β), chemokines, interferon alpha (IFN-α), interferon gamma (IFN-γ), IL-1β, IL-6, IL-8, and other pro-inflammatory cytokines are released from immune effector cells more easily when TNF-α is present. Moreover, when pro-inflammatory cytokines or bacterial lipopolysaccharide (LPS) activate the cell under heightened inflammation situations, inducible nitric oxide synthase (iNOS) is induced. Numerous signaling pathways are involved in the signal transduction of inflammatory reactions, such as the nuclear factor kappa B (NFκB), the toll-like receptor (TLR), Janus kinase/signal regulators and stimulants of transcription (JAK-STAT), and mitogen-activated protein kinase (MAPK) pathways. These pathways are activated by a sequence of phosphorylation events that result in the production of adhesion molecules, cytokines, and chemokines as well as the regulation of several anti-apoptotic target genes [32].
- Immunosuppressive effects on astrocytes. It is the astrocytes that are targeted by the immunosuppressive properties of cannabinoids. Astrocytes, which make up 60-70% of the central nervous system, are important for neuronal development, communication, glucose metabolism and glutamate elimination [33]. As an illness advances, astrocytes become active and release nitric oxide, chemokines, and cytokines, which all help to enhance the body's inflammatory reaction. Many researchers looked at the potential inhibitory effect of cannabis on astrocytes in the setting of multiple sclerosis, as these cells possess both CB1 and CB2 receptors. According to a study, anandamide (AEA) affects primary murine astrocytes that have been triggered by Theiler's murine encephalomyelitis virus (TMEV). AEA activated astrocytes through a CB1-mediated route, prompting the generation of IL-6. IL-6 release has been shown to enhance the synthesis of neuronal growth factors, albeit its exact function in the central nervous system is yet unknown. Furthermore, it has been demonstrated that glial cells activated by IFN-γ/IL-1β produce less TNF-α when exposed to IL-6 [34]. In a second

investigation, researchers demonstrated that AEA as well as the synthetic CB1 agonist CP-55940 reduced the generation of nitric oxide by LPS-stimulated astrocytes obtained from mice that were one day old in a way that was CB1-dependent. Human fetal astrocytes have been shown to exhibit both CB1 and CB2 receptors, as well as WIN55,212-2, which has been shown to reduce inflammatory products such as nitric oxide, TNF-α, CXCL10, CCL2, and CCL5 [35].

- **Endocannabinoid system modulation.** Endocannabinoids, their metabolizing and degrading enzymes, and endocannabinoid receptors are expressed by the majority of immune cells. In these cells, the CB2 receptor is expressed 10-100 times more strongly than the CB1 receptor, which is also present, although to a lesser extent. Additionally, anti-inflammatory reactions are regulated by CB receptor activation. The release of pro-inflammatory cytokines IL-12 and IL-23 from cultivated activated macrophages was reduced while the release of anti-inflammatory cytokine IL-10 was elevated upon activation of CB2 receptors by their agonist. Extracellular signal-regulated kinases (ERK1/2-MAPK) mediated the inhibitory impact of CB2 on IL-12 production. Another research showed that a CB2 receptor agonist decreased the phosphorylation of ERK1/2 and NF-kB-p65 caused by LPS in human mononuclear cells from the peripheral blood, as well as the production of pro-inflammatory cytokines such as TNF-α, IL-1β, IL-6, and IL-8. Using a naive CD4+ T lymphocyte community isolated from a mouse spleen, a selective/inverse CB2 agonist prompted Th0 cells to differentiate into regulated T cells (Treg) cell phenotypes. T cell multiplication and cytokine generation are both impeded by the Treg phenotype, which plays a key role in immunity suppression. FoxP3, TGF-β, and IL-10 expression were the hallmarks of the Treg phenotype, which was activated by signal transducer and activator of transcription 5A (STAT5A) and P38 protein phosphorylation. *In vivo,* colitis severity was thereby decreased by therapy using this CB2 selective/inverse agonist [5].
- **Lipid mediators inhibition.** Significant quantities of cyclooxygenase 2 (COX2), which initiates the transformation of arachidonic acid into prostaglandins (PGs), prostacyclin, and thromboxane A2, are produced when inducing an increase in impurity and iNOS levels. By blocking COX-2, cannabinoids can lower the synthesis of pro-inflammatory mediators generated from arachidonic acid, such as prostaglandins and leukotrienes [31].

Antioxidant effects of cannabis-derived compounds

Cannabis-derived compounds, including cannabinoids and terpenes, exhibit notable antioxidant properties as depicted in fig. 7. CBD, in particular, has demonstrated its ability to counteract oxidative stress by scavenging free radicals and enhancing the activity of endogenous antioxidant systems [36]. The diverse range of antioxidants in cannabis contributes to its overall antioxidative potential, offering neuroprotective effects and potential benefits in conditions associated with oxidative damage. The interplay between cannabinoids and oxidative stress pathways showcases the multifaceted antioxidant capabilities of cannabis-derived compounds [37].

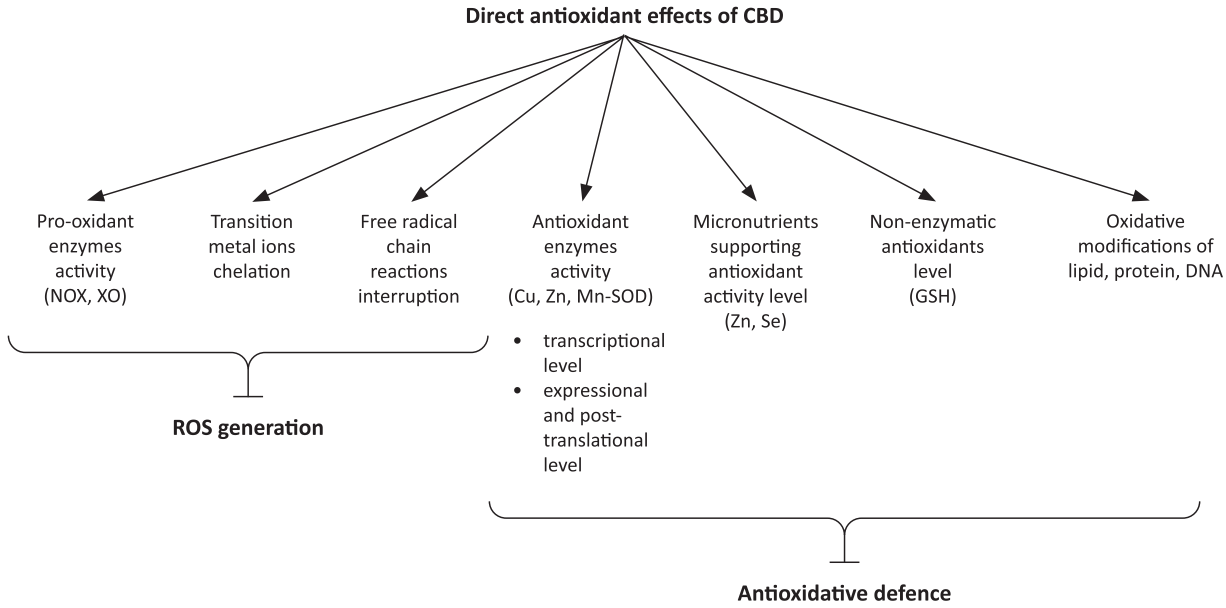


Fig. 7 The rapid antioxidant properties of CBD **Source:** [38]

- **Scavenging for free radicals.** CBD is an efficient agent for scavenging free radicals. It shields cellular constituents including lipids, proteins, and DNA from oxidative damage by neutralizing reactive oxygen species (ROS) and reactive nitrogen species (RNS). THC also exhibits antioxidant properties, although to a lesser extent than CBD. THC and CBD scavenge free radicals, which significantly reduces oxidative stress [38].
- **Increased expression of antioxidant enzymes.** Superoxide dismutase (SOD), the enzyme catalase along with glutathione peroxidase are examples of natural antioxidant enzymes whose activity can be increased by CBD. As a result, the skin is better protected against oxidative damage [38].
- **Lipid peroxidation prevention.** Cannabis inhibits the skin's lipids from peroxiding. Free radicals degrade triglycerides in cell membranes through a process called lipid peroxidation, which results in cell damage. Cannabinoids support the firmness of skin cells by blocking this process.
- **Reduction of inflammation caused by oxidative stress.** Cannabinoids attenuate oxidative stress by inhibiting the activation of the inflammatory processes that are triggered by ROS. They are particularly beneficial for skin health due to their synergistic anti-inflammatory and antioxidant properties. [38].
- **Safety from UV rays.** One of the main causes of oxidative damage in the skin is UV radiation exposure. By absorbing UV rays and destroying the free radicals they produce, CBD has been demonstrated to shield skin cells from UV-induced damage [38].

Implications for inflammatory skin disorders

The implications of cannabinoids in the context of inflammatory skin disorders are gaining attention in both preclinical and clinical studies. CBD, with its anti-inflammatory and antioxidant properties, holds promise for conditions like psoriasis, eczema, and dermatitis. The modulation of inflammatory responses and the protection against oxidative stress suggest a potential therapeutic role for cannabis-derived compounds in managing skin disorders [39]. Additionally, the interaction with the ECS in skin cells further underscores the relevance of cannabinoids in addressing inflammatory skin conditions [42]. Further research is warranted to explore the specific mechanisms and optimal formulations for effective dermatological applications.

- Management of dermatological disorders
  - **Acne and sebum regulation.** The regulation of sebum in acne management has led to the emergence of cannabinoids as potential therapeutic agents. CBD, with its anti-inflammatory and sebostatic properties, has effectively controlled sebum production. CBD's modulation of the ECS and its interaction with sebaceous glands indicate a promising approach for treating acne [41]. The anti-inflammatory effects also play a role in reducing acne lesions and preventing further breakouts [42]. Preliminary research suggests the potential of cannabinoids in formulating innovative acne treatment approaches.
  - **Psoriasis and eczema.** Cannabis-derived compounds, particularly cannabinoids, have shown promise in managing psoriasis and eczema [43]. Both CBD and THC exhibit anti-inflammatory properties, which can alleviate symptoms associated with these skin conditions. The immunomodulatory effects of cannabinoids contribute to their efficacy in reducing inflammation, itching, and skin lesions. Topical applications of cannabis-derived products have been explored, showing potential for localized relief without the psychoactive effects of THC [42]. As research advances, cannabis-based formulations may become valuable additions to the therapeutic arsenal for psoriasis and eczema.
  - **Anti-aging properties and collagen synthesis.** The anti-ageing potential of cannabis-derived compounds is a subject of growing interest. Cannabinoids, such as CBD, demonstrate antioxidant properties that combat oxidative stress, a key purpose of skin ageing. Moreover, cannabinoids may influence collagen synthesis, contributing to skin elasticity and firmness [44]. By interacting with the ECS and other cellular pathways, these compounds may promote skin health and mitigate signs of ageing. While more studies are needed to establish the specific mechanisms and optimal formulations, the preliminary findings suggest that cannabis-derived compounds hold promise in the realm of anti-ageing skincare.
- Formulation challenges and solutions
  - **Ensuring the stability of cannabis-derived compounds** in cosmeceutical formulations poses a significant challenge due to their susceptibility to degradation caused by factors like light, heat, and oxygen [45]. Due to above, formulators may utilise innovative encapsulation techniques, such as liposomes or microencapsulation, to shield these compounds from external influences and enhance their stability over time [46].
  - **Delivery systems and bioavailability** are critical aspects when formulating cannabis-derived compounds for cosmeceutical use. Achieving optimal absorption and bioavailability requires careful consideration of formulation matrices, particle size, and carrier systems [47]. Nanotechnology and emulsion-based delivery systems can enhance the bioavailability of cannabinoids, ensuring their efficacy when applied to the skin.

- Combining cannabis extracts with traditional skincare ingredients necessitates thoughtful formulation to maximize synergistic benefits. Challenges may arise due to varying solubilities and interactions between cannabis compounds and traditional skincare ingredients. Formulators can overcome these challenges by conducting compatibility studies, adjusting formulation ratios, and leveraging advanced delivery systems to ensure harmonious integration and enhance overall skincare efficacy [47].

REGULATORY LANDSCAPE

Legal considerations surrounding cannabis-derived cosmeceuticals

- Overview of cannabis legalization. Discuss the legal status of cannabis and its derivatives in various regions and countries. Highlight any recent changes in legislation related to the use of cannabis in cosmetic and skincare products [48].
- Distinction between hemp and marijuana. Explore how regulations differentiate between hemp-derived and marijuana-derived products [48]. Explain the significance of the THC content in cannabis products and its impact on legality.
- Ingredient transparency and labelling requirements. Analyse the labelling regulations for cannabis-derived ingredients in cosmeceuticals. Discuss requirements for accurate ingredient lists, concentrations, and potential allergens.
- Quality control and testing standards. Explore the testing standards and quality control measures imposed on cannabis-derived ingredients in skincare products [49]. Discuss the importance of ensuring product safety and efficacy through rigorous testing.

Regulatory challenges and compliance

- Inconsistencies in regulations. address challenges arising from variations in cannabis regulations globally and within different regions of a country and how companies navigate these inconsistencies to ensure compliance [50].
- Navigating compliance with existing cosmetic regulations. Explore how companies align with existing cosmetic regulations while incorporating cannabis-derived ingredients [53]. Discuss the potential challenges in meeting both cannabis-specific and general cosmetic regulatory requirements.
- Research and development hurdles. Highlight the challenges faced during the research and development phase of cannabis-infused cosmeceuticals and the need for scientific studies to support claims and substantiate the safety and efficacy of these products [51].
- Consumer education and awareness. Emphasize the role of companies in educating consumers about the regulatory landscape and safety of cannabis-infused skincare products and the challenges in addressing misconceptions and building consumer trust [51].

Global perspectives on cannabis in skincare products:

- International market trends. Explore the growing trends in the global market for cannabis-infused skincare products, consumer preferences and market dynamics in different regions.
- Country-specific regulations. Provide an overview of how various countries approach the regulation of cannabis in skincare and cosmetic products [52]. Highlight any unique considerations or restrictions in specific regions.
- Collaboration and harmonization efforts. Discuss international efforts to harmonize regulations related to cannabis-derived cosmeceuticals. Explore collaborations between countries or regulatory bodies aiming for standardized guidelines.
- Future outlook and emerging markets. Offer insights into the potential evolution of global regulations for cannabis in skincare products. Identify emerging markets and regulatory trends that may shape the industry's future. In addressing these legal and regulatory aspects, stakeholders in the cannabis-derived cosmeceuticals industry can better navigate the complexities and contribute to the establishment of clear and consistent guidelines for the development and marketing of such products [52].

Consumer perception and education

- Public awareness and misconceptions. Assess the existing awareness and perceptions of consumers regarding the therapeutic potential of cannabis in cosmetics. Explore common misconceptions or myths that may exist among the general public [53]. Media influence and stigma and the impact of media portrayal on public perceptions of cannabis-infused cosmetics. Address any lingering stigma associated with cannabis and its potential effects on consumer attitudes.
- Scientific literacy and understanding. Evaluate the level of scientific literacy among consumers regarding the therapeutic properties of cannabis [52]. Identify areas where misunderstandings or lack of information may exist.

Marketing strategies and ethical considerations

- Marketing claims and compliance. Examine the marketing strategies employed by companies in promoting the therapeutic potential of cannabis in cosmetics and the importance of aligning marketing claims with scientific evidence and regulatory guidelines.

- Transparency in product communication. Explore ethical considerations related to transparent communication about the use of cannabis in cosmetic products and the role of clear labelling and information dissemination in building consumer trust.
- Avoiding exaggeration and false claims. Highlight the risks associated with exaggerating therapeutic claims related to cannabis in cosmetics and the ethical responsibility of companies in providing accurate information to consumers.
- Community engagement and social responsibility. Explore how companies engage with the community and demonstrate social responsibility in promoting cannabis-infused cosmetics and initiatives that contribute positively to public perceptions [54].

The role of education in promoting informed behaviour

- Consumer education initiatives. Discuss the need for educational campaigns to inform consumers about the therapeutic potential of cannabis in cosmetics. Highlight successful examples of initiatives aimed at dispelling myths and providing accurate information.
- Healthcare professional involvement. Explore the role of healthcare professionals in educating consumers about the benefits and risks of using cannabis-infused cosmetics and potential collaborations between the beauty industry and healthcare providers.
- Online and offline platforms for education. Identify effective platforms, such as websites, social media, or in-store materials, for educating consumers about cannabis in cosmetics and the role of influencers and experts in disseminating accurate information.
- Continuous learning and adaptation. Emphasize the importance of ongoing education as the scientific understanding of cannabis evolves. Discuss strategies for companies to adapt their educational efforts based on emerging research and changing perceptions. By addressing public awareness, ethical marketing, and education initiatives, the industry can foster a more informed consumer base, leading to responsible and confident choices regarding the use of cannabis-derived products in the cosmetic and skincare market [55].

FUTURE DIRECTIONS AND RESEARCH OPPORTUNITIES

Novel cannabis-derived compounds and extracts

- Identification and isolation. Explore potential novel compounds and extracts derived from cannabis with therapeutic properties for skincare and the advancements in technology and methodologies for the identification and isolation of these compounds.
- Synergistic formulations. Investigate opportunities for combining cannabis-derived compounds with other botanicals or ingredients to create synergistic formulations and the potential for enhancing efficacy and addressing a broader range of skincare concerns.
- Bioavailability and delivery systems. Explore research on improving the bioavailability of cannabis-derived compounds in cosmeceuticals and innovative delivery systems that enhance the absorption and effectiveness of these compounds [55].

Clinical trials and evidence-based cosmeceutical development:

- Clinical validation of efficacy. Highlight the importance of conducting rigorous clinical trials to validate the efficacy of cannabis-derived cosmeceuticals. Discuss specific parameters, such as anti-ageing, anti-inflammatory, or moisturizing effects, that can be measured objectively [55].
- Long-term safety assessments. Emphasize the need for long-term safety assessments to ensure the safety profile of cannabis-infused skincare products and methodologies for monitoring potential adverse effects over extended usage periods.
- Objective measurement tools. Explore the development and implementation of objective measurement tools for assessing improvements in skin health and appearance. Discuss the use of imaging techniques, biomarkers, or other quantifiable metrics in clinical trials.
- Inclusion of diverse study populations. Address the importance of including diverse study populations in clinical trials to understand the potential variations in responses across different skin types and ethnicities.

Collaborations between the cosmetic and medical industries:

- Integration of medical expertise. Explore opportunities for collaboration between cosmetic companies and medical professionals in the development of cannabis-derived cosmeceuticals and how medical expertise can contribute to the formulation and validation of products [55].
- Regulatory pathways for medical cosmeceuticals. Investigate regulatory pathways for products that bridge the gap between cosmetics and medical interventions and potential frameworks for regulatory approval for products with demonstrated therapeutic benefits.
- Cross-industry knowledge exchange. Emphasize the benefits of knowledge exchange between the cosmetic and medical industries and the forums, conferences, or

collaborative platforms that facilitate information sharing and interdisciplinary research.
- Consumer confidence and medical validation. Explore how collaborations with the medical industry can enhance consumer confidence by providing products with validated medical benefits. Discuss the potential impact on market positioning and consumer trust. As the field of cannabis-derived cosmeceuticals continues to evolve, these research directions and collaborations have the potential to shape the future of the industry, fostering innovation, scientific validation, and responsible product development.

Implications for the cosmeceutical industry

- Market expansion and differentiation. Discuss how the incorporation of cannabis-derived compounds in cosmeceuticals can lead to market expansion. Explore the potential for differentiation and competitive advantage for companies embracing these ingredients.
- Consumer demand and product innovation. Highlight the increasing consumer demand for natural and plant-based skincare products, driving the need for innovation in the cosmeceutical industry and how cannabis-derived compounds offer a unique selling proposition and contribute to product innovation [55].
- Regulatory compliance and standardization. Explore the challenges and opportunities related to regulatory compliance in the cosmeceutical industry, considering the evolving landscape of cannabis regulations. Discuss the importance of standardization in ensuring product quality and compliance with regional and global regulations.
- Brand image and market positioning. Analyse the impact of incorporating cannabis-derived compounds on a brand's image and market positioning. Discuss strategies for companies to communicate effectively and responsibly about their use of cannabis in cosmeceuticals.
- Partnerships and collaborations. Explore potential partnerships between cosmeceutical companies and cannabis producers, extractors, or researchers. Discuss how collaborations can enhance the development, testing, and marketing of cannabis-infused skincare products [55].

The future landscape of cannabis-derived compounds in skincare

- Customization and personalization. Investigate the trend towards customization and personalization in skincare products, considering the diverse array of cannabis-derived compounds available and how companies can tailor products to address specific skin concerns for individual consumers.
- Global market dynamics. Analyse the evolving dynamics of the global market for cannabis-infused skincare products and potential shifts in consumer preferences, market regulations, and emerging trends in different regions [56].
- Research and development innovations. Explore ongoing and future research initiatives focused on unlocking the full therapeutic potential of cannabis-derived compounds for skincare and the breakthroughs in R&D that can lead to the development of more advanced and effective cosmeceutical products.
- Consumer education and acceptance. Discuss the role of continued consumer education in shaping the future acceptance of cannabis-derived compounds in skincare. Explore how increased awareness and positive experiences can contribute to mainstream adoption.

As the cosmeceutical industry continues to navigate the integration of cannabis-derived compounds, careful consideration of these implications and a proactive approach to industry trends can position companies for success in a rapidly evolving market.

CONCLUSION

Overall, the application of cannabis's anti-inflammatory and antioxidant properties in cosmeceuticals seems to be a feasible approach. Cannabis active ingredients, particularly THC and CBD, offer extensive anti-inflammatory and antioxidant benefits in cosmeceuticals. The compounds in skincare products have the potential to alter the endocannabinoid system, reduce pro-inflammatory cytokines, and enhance endogenous defences against antioxidants. More studies are highlighting the effectiveness of components derived from cannabis in improving the function of the skin barrier, decreasing erythema, and lowering the appearance of ageing. Comprehensive clinical research is essential to demonstrate the long-term safety and efficacy of cannabis-based cosmeceuticals, despite these promising findings. The use of cannabis in cosmeceutical products is poised to emerge as a significant trend due to increasing consumer demand for safe, natural skincare solutions. Future research should focus on standardised formulations, optimal dosages, and comprehensive safety profiles to fully harness the medicinal potential of cannabis in cosmetics.

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