




Review

Bioactives in Nutricosmetics: A Focus on Caffeine from Tea to Coffee

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Abstract: Known for its stimulating effects on the nervous and cardiovascular systems, caffeine has proven remarkable versatile properties. It can be used in a wide range of different products, from anti-aging cosmetics to the pharmaceutical treatment of hair loss. Caffeine is known for its antioxidant properties and is commonly found in moisturising creams recommended as anti-aging or anti-cellulite and also for the treatment of different skin disorders, including androgenic alopecia. This bioactive is also described to be able to enhance the sunscreen scattering effect of well-known ultraviolet (UV) blockers. One of the major challenges remains its penetration capacity into deeper skin layers, which may be achieved by the use of nanosized delivery systems, yet without the risk of transdermal delivery. In this review, we discuss the nutraceutical value of caffeine in cosmetic products, so-called nutricosmetics, which grants this bioactive several advantages in several formulations, in comparison to other potential bioactives of nutricosmetic value. Furthermore, the disclosed effects of bioactives commonly found in coffee, tea, and their by-products are reviewed and discussed. The discussion concludes by highlighting the significant benefits of caffeine in the treatment of skin disorders and its potential to enhance and promote skin health.

Keywords: caffeine; coffee; coffee by-products; cosmetics; anti-aging; antioxidant



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1. Introduction

Caffeine (1,3,7-trimethylxanthine) is commonly consumed in beverages, such as coffee and tea, ranking as the second most widely consumed beverages globally, following water [1]. Caffeine is obtained from the coffee fruit. Historically, coffee production has mostly emphasised the cultivation of the beans, with the fruit either being used as fertiliser or often discarded as waste. This process results in substantial water pollution and carbon emissions, which disrupt the fragile ecology at its source. The coffee fruit holds great potential for a range of industries, being found in a variety of products, from juices, teas, and energy snacks to health and beauty products (Figure 1). Caffeine is being widely utilised in the food, pharmaceutical, and cosmetics industries due to its multifaceted properties. It is an alkaloid of interest for the pharmaceutical industry because of its stimulating properties on the nervous and cardiovascular systems [2]. It acts as a psychoactive stimulant, increasing cognition and awareness while suppressing fatigue. Caffeine can play dual roles, maintaining elevated attention levels on one hand and potentially leading to dependence with excessive use on the other [3]. Caffeine-based cosmetic products have also gained increasing interest in recent years. The use of caffeine as an active ingredient in cosmetic

products is attributed to its active role in hair growth, its anti-cellulite effects, antioxidant properties, and capacity to counteract photoaging in daily creams and beauty masks. When applied topically, caffeine reduces dark circles effectively through its vasoconstrictive action and attenuates wrinkles [4].

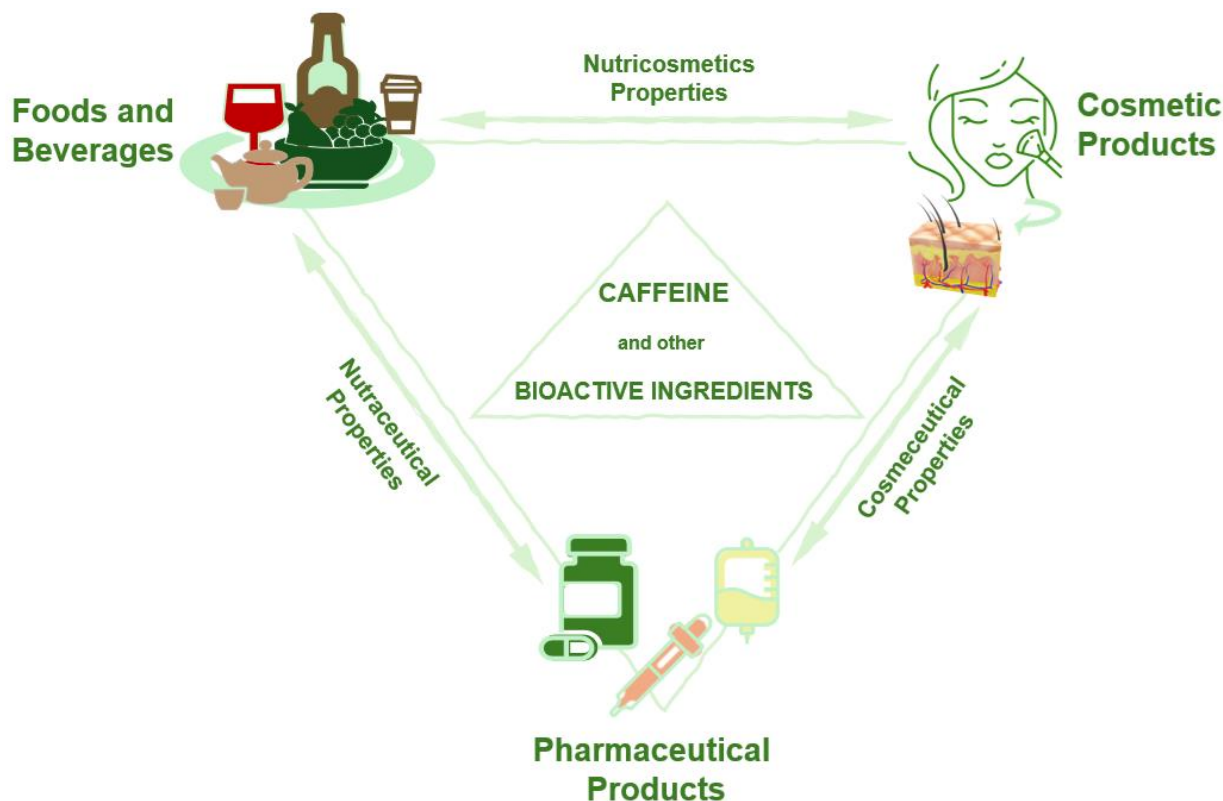


Figure 1. Illustration of the interplay of fields (foods and beverages, pharmaceuticals, and cosmetics) in which caffeine and other bioactive ingredients show a high market value.

Caffeine is employed in sunscreens to prevent UV radiation, assisting in treatments against cancer and UV-induced damage, as well as in the treatment of male androgenic alopecia and cellulite [5]. Several properties can be attributed to this bioactive ingredient, such as anti-oxidant, anti-inflammatory, and antimicrobial, which grant this bioactive a great deal of applications.

Given the well-documented benefits of caffeine to address various health and skin issues, the primary caffeine extraction remains focused on the coffee bean. However, to promote environmental sustainability in industrial applications, it is suggested that future studies focus on fulfilling this gap knowledge, considering the use of tea and coffee by-products, as their multiple biological activities have already been proven and discussed (see Section 2) [6–10]. Moreover, this study highlights the importance of caffeine and its related bioactives (found in coffee, tea, and their by-products) as nutricosmetics with a high market value.

In the process of caffeine extraction, several coffee by-products are obtained from many stages of the manufacturing pathway, ranging from post-harvest processing to roasting and coffee consumption [11]. The by-products consist of substandard coffee beans, husks/pulp, parchment, silverskin, and spent coffee grounds, containing multiple bioactives such as caffeine, caffeic acid, chlorogenic acid, trigonelline, cafestol, and kahweol [12–15].

Coffee silverskin and spent coffee grounds are the two most extensively researched by-products derived from the process of making coffee. The coffee silverskin is a thin layer that surrounds the green coffee seeds. It separates from the beans during the heating process and is the only waste product produced during roasting. Currently, it is primarily utilised as a fertiliser or fuel source, making its valorisation essential.

Silverskin has a significant amount of dietary fibre (56–62%) and is also abundant in protein (16–19%) and minerals, specifically potassium, magnesium, and calcium [11]. This by-product also has a low water content, which enhances its stability, and a low-fat content (2–4%), primarily consisting of saturated fatty acids. The antioxidant properties of silverskin are primarily attributed to its phenolic composition, particularly chlorogenic acids and their derivatives. Furthermore, the presence of tocopherols (α , β , γ , and δ) and tocotrienols (β , γ , and δ) was detected in coffee silverskin. Among these, α -tocopherol was determined to be the predominant form [11].

The majority of spent coffee grounds are presently being burned or disposed of in landfills, and alternative applications for this by-product are being considered, not only in skincare products, but also in the realms of food ingredients, biofuel, adsorbents, bioplastics, and materials for the building industry. Different from coffee silverskin, spent coffee grounds contain a high content of moisture, while being solid and similar to coffee silverskin in containing a considerable content of fibre, protein (14–17%), hemicellulose, and minerals (e.g., potassium and magnesium) [11]. The abundance of bioactives that can be obtained from these by-products is greatly influenced by the extraction process. Figure 2 illustrates different industrial processes of coffee beans, the predominant bioactives mainly found in coffee and its by-products, and their potential bioactivities with nutricosmetic value.

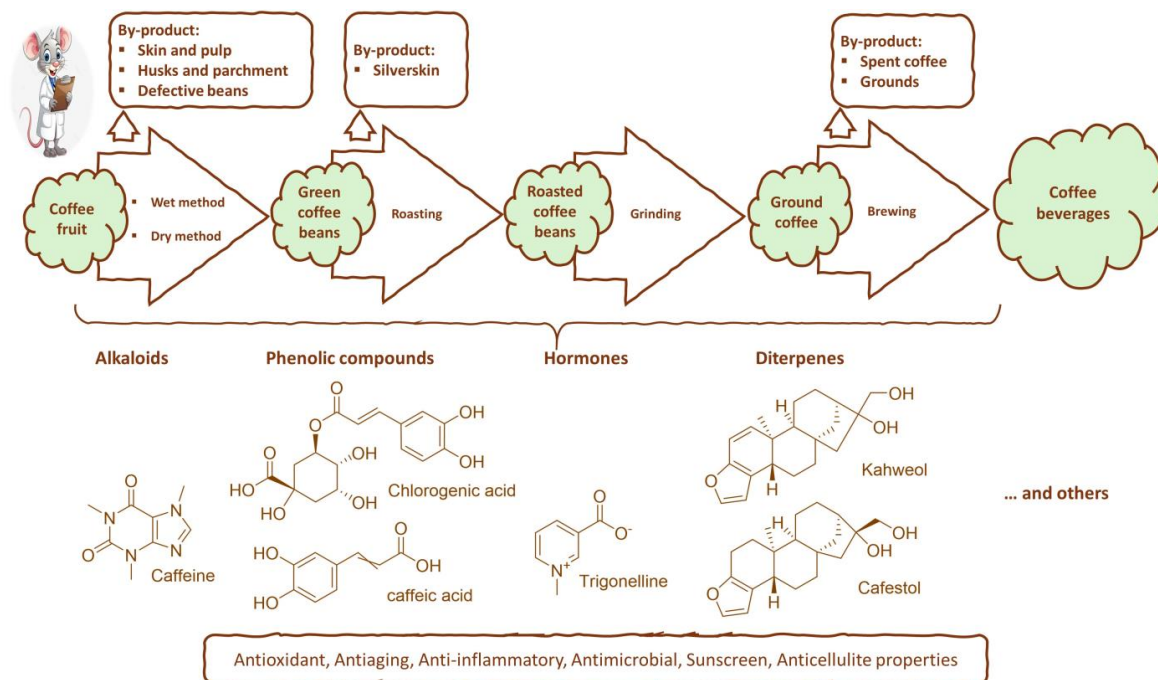


Figure 2. Industrial steps encountered in the process of transforming coffee fruit into coffee beverages, during which several other bioactives and by-products of nutricosmetic value besides caffeine can be obtained.

The efficacy of bioactives found in cosmetics or pharmaceuticals in affecting cellular metabolism and other skin processes is mostly determined by their ability to penetrate deeper in the skin layers, yet without reaching systemic circulation [16].

Prior research has determined that the ability of caffeine to pass through the skin barrier remains unaffected by occlusion and skin thickness. However, when a 5% caffeine solution in a hydroxyethyl cellulose gel was applied for 7 days, it notably decreased the amount of water lost through the skin in males compared to females. The highest rates of caffeine absorption via the human skin were determined to be $2.24 \pm 1.43 \mu\text{g}/\text{cm}^2/\text{h}$, while the maximum absorption occurred 100 min after local administration *in vivo* [17].

Touitou et al. (1994) [18] conducted a study employing quantitative skin autoradiography and discovered that after 24 h, the highest concentration of caffeine ($280 \mu\text{g}/\text{tissue}$)

alopecia, drug targeting, therapy effect). We found that several approaches for the recovery of its by-products are possible through the development of innovative nanoparticles made of different types of polymers. Recent research shows that the combination of both caffeine and nanoparticles holds enormous potential for applications in cosmetic formulations.

2. Bioactives-Composed Nutricosmetics

Nutricosmetics represent an innovative category within the cosmetics field, distinguished by their ability to deliver bioactive compounds to deeper layers of the skin without reaching systemic circulation. Unlike cosmetic products, which primarily focus on enhancing the superficial appearance of the skin, topical pharmaceuticals are designed to provide therapeutic effects that extend beyond the skin's surface. Several bioactive compounds, coming from natural sources such as plants, marine organisms, and microorganisms, have unique properties with diverse therapeutic benefits that add nutritional value to the skin [19,22–24]. This section explores the mechanisms, benefits, and potential applications of bioactives in dermatopharmaceuticals, with a focus on sources related to caffeine (e.g., coffee, tea, and their by-products).

Bioactive compounds exert their effects through various mechanisms, depending on their chemical nature and target pathways. Common mechanisms include antioxidant activity, anti-inflammatory effects, modulation of cellular signalling pathways, and antimicrobial properties. For instance, polyphenols from green tea exhibit strong antioxidant properties, protecting skin cells from oxidative stress and UV-induced damage.

Other bioactives derived from natural sources, including hydroxybenzoic acid derivatives (caffeic acid and chlorogenic acid), polyphenols (chlorogenic acid), alkaloid hormones (trigonelline), and diterpens (cafestol and kahweol) [15], offer significant potential as active ingredients for systemic delivery through transdermal formulations in dermatopharmaceuticals.

Table 1 presents examples of bioactives used in nutricosmetics and potential side effects found in coffee, tea, and their by-products. These compounds are incorporated into patches or other transdermal systems that allow them to penetrate the skin and enter the bloodstream. This approach not only facilitates targeted therapy for conditions like chronic pain, inflammation, and cardiovascular health, but also minimises the gastrointestinal side effects commonly associated with oral medications [25–28].

It has been reported that coffee silverskin is a promising source of bioactives for use in dermocosmetic products, particularly as nutricosmetics, due to its high antioxidant potential. This efficacy may be attributed to the synergistic interaction of chlorogenic acids, caffeine, and melanoidins, which are the primary bioactives found in coffee silverskin, along with other antioxidant compounds. Bioactives from coffee silverskin have demonstrated benefits for skin appearance, including anti-aging, anti-inflammatory, antimicrobial, anti-cellulite, and anti-hair loss effects, as well as UV protection [6,7].

Bioactives in spent coffee grounds offer multiple health benefits, including fatty acids such as linoleic acid (with an unsaturated to saturated fatty acid ratio of 33.12), protein, minerals, hemicellulose, caffeine, and polyphenols (including chlorogenic acid and tannins), as well as fibres. Spent coffee grounds have been reported to possess antioxidant, anti-aging, anti-inflammatory, and antimicrobial properties, and they also provide UV protection, similar to sunscreen [8–10]. These properties contribute to addressing related health issues and promoting environmental sustainability in industrial applications [6–10]. By leveraging the natural properties of these bioactive compounds, dermatopharmaceuticals provide a non-invasive and effective alternative for treating various health conditions.

Ongoing research in the field of bioactives-composed dermatopharmaceuticals is crucial for discovering new compounds and optimising their delivery. Advances in nanotechnology, for instance, have improved the stability and delivery of bioactives, ensuring more effective skin penetration and prolonged activity in the skin [29–32]. Additionally, understanding the synergistic effects of combining different bioactives can lead to more comprehensive and effective skincare solutions [19,33,34].

Table 1. Examples of bioactives used in nutricosmetics and potential side effects.

Bioactives	Sources	Applications	Side Effects	References
Caffeine	Different sources	It stimulates the blood circulation around the eyes, which may help to improve the look of dark circles and puffy under-eyes. Also, it may reduce photo damage, fine lines, wrinkles, and the appearance of cellulite.	Products with high concentrations of caffeine may cause redness, stinging, or burning in sensitive skin	[16,35,36]
Chlorogenic acid	-	Its influence on skin functions, particularly concerning the dermal collagen net-work and the epidermal skin barrier, remains unclear (skin damages). Chlorogenic acid treatment on human dermal fibroblast Hs68 cell can promote the production of procollagen type I. It enhances the expression of skin barrier genes, including those encoding filaggrin, involucrin, and envoplakin, in epidermal keratinocytes. Additionally, it induces a complex response in the cytokine profile of these keratinocytes.	Not mentioned	[12]
Caffeic acid and chlorogenic acid	Coffee bean and by-products	Coffee pulp extract exhibited significant free radical scavenging activity, inhibited tyrosinase, and improved skin health in healthy subjects. Furthermore, the in vivo findings suggest that supplementation with coffee pulp extract enhances skin moisture, brightness, elasticity, and collagen content while reducing spots, texture irregularities, wrinkles, and pores.	Not mentioned	[13]
Trigonelline	Purified	It may have potential as an anti-obesity actor, while it has antidiabetic and anticancer effects.	Not mentioned	[14]
Cafestol and kahweol	Coffee bean and by-products	They decreased extracellular melanin levels in B16F10 cells and lowered dendritic parameters in human melanocytes, showcasing their distinct potential to target extracellular melanogenesis and melanin export. This suggests they could serve as a promising candidate for treating hyperpigmentation disorders in human skin, with applications in both clinical and cosmetic settings.	Not mentioned	[15]
Tree oil	Tea	It is used to treat acne, fungal infections (such as athlete's foot), and minor cuts and abrasions due to its antimicrobial properties.	Tea tree oil can cause skin irritation, allergic reactions, and dryness, particularly if used undiluted	[29,31,37,38]
Polyphenols	Green Tea	Green tea polyphenol patches are used for their antioxidant and anti-inflammatory properties to treat conditions like psoriasis and dermatitis. The patches deliver polyphenols transdermally to reduce inflammation and oxidative stress.	Green tea polyphenols are typically well-tolerated, but potential side effects include skin irritation, redness, and itching at the application site	[39–41]

Table 1. Cont.

Bioactives	Sources	Applications	Side Effects	References
Polyphenols (green and black tea)	<i>Camellia sinensis</i>	Black and green tea polyphenols alleviate UV-induced damage in human skin. Both extracts adsorb UV radiation and have the potential to repair UV deep skin damage due to their high antioxidant activities.	Not mentioned	[42]
Polyphenols	<i>Camellia sinensis</i> (L.) Kuntze	The polyphenol-rich extract of green tea exhibited anti-aging effects on B16F10 melanoma cells and human skin fibroblasts by inhibition of the tyrosinase and tyrosinase-related protein-2 activities. The enzyme inhibitory effect (MMP-2) is greater than vitamin C.	Not mentioned	[43]

In general, the use of bioactives in cosmetics offers several benefits [12–16,35,36,42–46]:

- **Enhanced Skin Protection:** Bioactive compounds like polyphenols (found in tea and coffee) and vitamins C and E are powerful antioxidants that protect the skin from environmental stressors, such as UV radiation and pollution.
- **Anti-Aging Properties:** Many bioactives, including retinoids, peptides, and polyphenols (found in tea and coffee), stimulate collagen production and promote cell turnover, reducing the appearance of fine lines and wrinkles.
- **Anti-Inflammatory Effects:** Bioactives such as polyphenols can reduce skin inflammation, making them effective in treating conditions like eczema and psoriasis.
- **Antimicrobial Activity:** Bioactives found in tea tree oil and honey possess natural antimicrobial properties, useful in managing acne and other microbial infections.
- **Skin Brightening:** Bioactives such as cafestol, kahweol, caffeic, chlorogenic acid, and kojic acid inhibit melanin production, helping to even out the skin tone and reduce hyperpigmentation.

About applications in skincare products, bioactives are incorporated into a variety of skincare products, including creams, serums, lotions, and cleansers. These products are formulated to target specific skin concerns, from aging and hyperpigmentation to acne and sensitivity. For instance [13,33,47,48],

- **Anti-Aging Creams:** Often contain bioactives like retinoids, peptides, and antioxidants (polyphenols) to reduce wrinkles and improve skin elasticity.
- **Brightening Serums:** Typically include polyphenols (found in tea and coffee), vitamin C, niacinamide, and botanical extracts to lighten dark spots and enhance radiance.
- **Acne Treatments:** Use bioactives such as salicylic acid, benzoyl peroxide, and tea tree oil to clear pores and reduce inflammation.

3. Caffeine-Composed Nutricosmetics

In recent years, caffeine-composed cosmetics have gained significant popularity due to their unique benefits and effectiveness [16,49]. Bioactive compounds, including caffeine, have become a crucial component in skincare formulations, offering a range of advantages for skin health and appearance. From enhanced skin protection to anti-aging properties and anti-inflammatory effects, these bioactives are transforming the cosmetic industry and providing consumers with innovative solutions for their skincare needs. Focusing on caffeine and its mechanisms of action, it is important to highlight the following [5,16]:

- **Stimulation of Microcirculation:** Caffeine improves skin microcirculation, increasing blood flow and facilitating the oxygenation and nutrition of tissues, which can contribute to a reduction in cellulite and improvements in hair health.
- **Inhibition of Phosphodiesterase:** As a phosphodiesterase inhibitor, caffeine elevates cyclic AMP levels in cells, modulating various signalling pathways and reducing inflammation. Additionally, caffeine has been found to inhibit collagenase, elastase, and tyrosinase enzymes, which are involved in skin aging and pigmentation processes.
- **Antioxidant Effects:** Caffeine neutralises free radicals, protecting skin cells from oxidative damage induced by environmental factors such as UV radiation and pollution.

Studies have shown that caffeine, when topically applied, can have significant impacts. For instance, topical applications of caffeine or caffeine sodium benzoate have been found to enhance UVB-induced apoptosis and inhibit UVB-induced skin carcinogenesis; it was found that topical application of caffeine sodium benzoate immediately after UVB exposure was 2 to 3-fold more potent than caffeine at enhancing UVB-induced apoptosis [50]. Additionally, caffeine was shown to decrease phospho-Chk1 levels and increase mitotic cells with cyclin B1 and caspase 3 in UVB-treated mice, indicating its potential role in tumour suppression [51]. Furthermore, caffeine has been demonstrated to promote apoptosis after UV treatment in primary human keratinocytes, suggesting a potential basis for its protective effects against UV radiation [52]. The role of hair follicles in the percutaneous absorption of caffeine has been investigated, highlighting the importance of follicular

penetration in the transcutaneous absorption of topically applied substances [53]. This finding underscores the significance of understanding the mechanisms of absorption for effective topical caffeine delivery.

Furthermore, two trials were conducted with topical caffeine solutions, one compared to a topical minoxidil solution and the other a combination of caffeine and minoxidil. The solution containing 0.2% caffeine exhibited results comparable to those of 5% minoxidil, showing an improvement of 10.59% in the caffeine group and 11.68% in the minoxidil group [54]. In addition, the combination of both caffeine and minoxidil was also observed in five individuals with androgenic alopecia, who were given a topical solution for application twice daily for 180 days. The formula contained 10% minoxidil, 0.2% biotin, a hydroalcoholic solution of 0.05% caffeine citrate, and 0.1% finasteride. At the end of 6 months, it was possible to observe a hair density growth of +1.05 in the individuals under study [54].

Another advantage of using caffeine for this type of treatment is the fact that there are virtually no side effects when compared to other tested products [55,56]. A comparison was made between a topical formulation of 3% propacil with caffeine and zinc for hair loss in men with androgenic alopecia. Nineteen men aged between 18 and 57 years old were enrolled in the study. The solution was applied for 12 consecutive weeks and was administered once daily. After the 12 weeks, combing tests showed results indicating a 26.9% decrease in hair loss which, compared to formulations using only caffeine where the greatest effectiveness occurred after 6 months of use, was 13.15% [57]. The results obtained are attributed to the synergistic properties of caffeine and procapil when combined, as caffeine acts as an inhibitor of the phosphodiesterase enzyme at the intracellular level, which regulates cyclic nucleotides, resulting in a decrease induced by testosterone as well as the 5- α -reductase enzyme [57]. In procapil, there is inhibition of the 5 α 1 and 5 α 2 reductase enzymes because the formula contains oleic acid that has vasodilator properties, and biotin, which helps to prevent hair loss and weakening [58,59]. The ability of caffeine to act as an ally of androgenic alopecia was evidenced, whether in solutions where the active ingredient is isolated or in combination with topical medications [57]. One of the major advantages of caffeine compared to other natural bioactives is its limited side effects. Another advantage of the topical use of caffeine is its ability to achieve results similar to topical medications available on the market and to enhance other formulations.

Scientific research also reports that caffeine in cosmetic formulations can prevent excessive fat accumulation in the skin, promote lymphatic drainage, protect the skin from photodamage, and enhance microcirculation [16,60]. Additionally, caffeine has been found to have a protective effect against UV radiation, reduce the formation of free radicals in skin cells, and potentially aid in preventing UV-induced skin cancers [16]. Furthermore, the encapsulation of caffeine in porous metal-organic frameworks has shown promising results, with exceptional payloads of up to 50 wt % and controlled release properties depending on the stability of the framework and interactions with caffeine [61].

Moreover, the use of caffeine in cosmetics is supported by its skin care properties, such as preventing excess fat storage in cells and its antioxidant effects [62]. Caffeine has also been incorporated into cosmetic formulations containing nanoencapsulated antioxidants, showing potential anti-aging effects and skin-barrier functionality improvements [63,64]. Additionally, scalp applications containing caffeine have been found to improve scalp condition and reduce hair shedding, indicating its potential benefits in hair care products [65].

Interestingly, the effectiveness of sunscreens containing caffeine against UV radiation was investigated [66]. UV radiation is one of the main causes leading to the development of melanoma on the skin. In the study, 12 volunteers, both men and women, participated. The use of an oil-in-water emulsion composed of ethylhexyl methoxycinnamate (7.5%), titanium dioxide (3.0%), and avobenzone (5.0%) without caffeine was compared to another emulsion with the same concentrations but with the addition of caffeine (2.5%) [49]. The sun protection factor (SPF) was determined both *in vitro* and *in vivo*. Caffeine could increase the SPF from 36 to 51 after sun exposure *in vitro*, whereas *in vivo* the SPF value

increased from 15.49 to 19.34. Alone, caffeine did not provide significant UV protection by itself, but when combined with sunscreens, it enhanced protection, largely due to its anti-inflammatory or antioxidant capabilities [49].

Kichou et al. (2023) [67] compared caffeine and α -tocopherol emulsions in terms of their penetration into human skin with and without the addition of emulsifying surfactants in both emulsions. Test samples were collected from female donors who underwent skin surgery on the chest area, with a thickness of ~ 500 μm and a diameter of 20 mm. For the caffeine tests, all women were Caucasian, aged 39, 40, and 55 years old, while for the α -tocopherol tests, the human skin samples were obtained from two Caucasian women aged 21 and 55, and one North African woman aged 51 [67]. One of the parameters analysed was the average particle size to assess penetration into the skin. The particles were analysed at 10%, 50%, and 90%, corresponding to D10, D50, and D90, respectively [67]. The D10 particles of caffeine had similar results, with values below 0.519 μm , while α -tocopherol had values of 0.561 μm . In the D50 particles, α -tocopherol had a value of 1.165 μm , indicating that 50% of the particles had a lower value, while for caffeine, it was 1.122 μm . In the D90 particles, α -tocopherol had a value of 2.321 μm , indicating that 90% of the particles had a lower value, whereas for caffeine, the value was 2.500 μm [67]. In the conducted study, both the caffeine and α -tocopherol emulsions demonstrate promising results for surfactant-free formulations, as they show the ability to deliver caffeine to human skin with an efficacy equivalent to that of a traditional emulsion. Table 2 shows some important examples of nanocarriers being proposed to enhance the skin penetration capacity of caffeine.

Table 2. Some most updated nanocarriers developed to enhance the skin penetration capacity of caffeine.

Nanocarriers	Highlighted Outcomes	References
NLC	<ul style="list-style-type: none"> ■ Enhance retention of caffeine 2 to 1.4-fold in 4 h; ■ Enhance the cellulite treatment, in vivo. 	[68]
Liposome	<ul style="list-style-type: none"> ■ Enhance the stability and skin penetration of caffeine in coffee berry extract; ■ Reduce toxicity and maintain its anti-aging effect. 	[69]
Cerosomes	<ul style="list-style-type: none"> ■ Enhance deposition of caffeine on the skin compared with gel-loaded caffeine, in vivo; ■ No evidence of irritation was observed, in vivo. 	[70]
Hydrogel	<ul style="list-style-type: none"> ■ The most significant healing was observed from hydrogel (PVA/aloe vera)-loaded caffeine and vitamin C, in vitro; ■ Successful re-epithelialisation was observed in wounds membranes, in vitro. 	[71]

Captions: NLC, Nanostructured lipid nanocarriers; PVA, Poly vinyl alcohol.

4. Conclusions

The use of caffeine and other bioactives extracted from tea, coffee, and their by-products as nutricosmetic ingredients proves to be highly advantageous. Caffeine has shown to be quite useful in addressing hair loss issues like androgenic alopecia, demonstrating very positive results compared to other active ingredients on the market. Its recent research applications in sunscreens due to its ability to prevent UV radiation from penetrating the skin with such intensity showcase the versatility of caffeine. The reviewed studies highlight caffeine's role in stimulating microcirculation and increasing blood flow, which facilitates tissue oxygenation and nutrition, contributing to the reduction in cellulite. Additionally, it has been demonstrated that caffeine inhibits the enzymes collagenase, elastase, and tyrosinase, which are involved in skin aging and pigmentation processes, therefore having anti-aging activity, thus making this bioactive interesting for several dermatological and cosmetic applications. However, one of the major challenges of using caffeine is its ability to penetrate the deeper layers of the dermis. Delivery systems prove to be a great ally in this regard, helping caffeine to penetrate the skin more deeply and yielding more positive results than intended. Moving forward, further research and development

in caffeine-based formulations promises continued innovation in enhancing therapeutic outcomes and meeting consumer demands in the skincare industry.

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