Review

Exploring Phenolic Compounds in Crop By-Products for Cosmetic Efficacy

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Exploring Phenolic Compounds in Crop By-Products for Cosmetic Efficacy

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Abstract: Phenolic compounds represent a group of secondary metabolites that serve essential functions in plants. Beyond their positive impact on plant, these phenolic metabolites, often referred to as polyphenols, possess a range of biological properties that can promote skin health. Scientific research indicates that using phenolics derived from plants topically can be advantageous, but the activity and stability highly depend on storage of the source material and the extract method. These compounds have the ability to relieve symptoms and hinder the progression of different skin diseases. Because they come from natural sources and have minimal toxicity, phenolic compounds show potential in addressing the causes and effects of skin aging, skin diseases, and various types of skin damage, such as wounds and burns. Hence, this review provides an extensive information of the particular crops from which by-product phenolic compounds can be sourced, but pointing the need investigation according to a proper storage plant material and the choice of the best extracting method, along with an examination of their specific functions and the mechanisms by which they act to protect skin.

Keywords: secondary metabolites; phenolic; skin; cosmetic; antioxidant

1. Introduction

Some plant by-products are rich in phenolic compound, which has been described as effective agents for health acting against environmental oxidative stressors. In this way, there is an increasing attention devoted to the development of cosmetic formulations allowing for higher stability and bioavailability of bioactive phenols [1]. Phenolic compounds stand out as a crucial category of plant secondary metabolites, playing a significant role in morphological development, physiological processes, and reproduction. Their synthesis occured through the pentose phosphate, shikimate, and phenylpropanoid pathways. The diverse biological properties of phenolics, attributed to their molecular structure, are well-recognized. The majority of phenolic compounds structure comprise at least one phenol ring, typically with hydrogen replaced by a more reactive residue like hydroxyl, methyl, or acetyl [2].

In this review, we establish the relationship between external application of plant phenolic compounds and human skin health. The contributions reviewed open new perspectives toward the exploitation of phenol-rich natural extracts obtained from plant by product as functional ingredients in the cosmetic sector, taking into account usual Mediterranean crops and pointing to the gasp in the knowledge that should be solved for taking these extracts into consideration in cosmetic sector.

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2. Composition in Phenolic Compounds of By-Products

A great diversity of phenolic compounds is found in the by-products of various crops such as artichoke, broccoli, cauliflower, citrus, grape, tomato, onion, and mushroom. Phenolic compounds can be extracted from different parts of plants, such as fruits, leaves, stems, roots, seeds, and flowers, and often these parts are considered by-products or wastes in the food industry and agriculture [3–6]. The type and content of these phenolic compounds in by-products depend on several factors, such as plant species, cultivar, maturity stage, processing method, storage condition, and extraction technique [5,7,8]. The main phenolic compounds found in some crop by-products are described below and summarized in Table 1.

Artichoke (*Cynara scolymus* L.) is a vegetable commonly found in Mediterranean areas, whose edible parts are the immature inflorescences called heads or capitula. To prepare fresh, canned, or frozen artichoke products, the outer parts, stems, and bracts are removed, generating these by-products that comprise 70% to 80% of the total artichoke head. However, a significant portion of the plant, including leaves, and stems is discarded during industrial processing, despite containing valuable bioactive compounds such as phenolic acids and flavonoids [5,9]. Chlorogenic and cynarin acid are the predominant phenolic compounds found in artichoke, while luteolin and apigenin derivatives are normally present [10–12]. The content and composition of these compounds vary depending on the part of the plant. Thus, the highest concentration of phenolic compounds is typically found in the parts closest to the artichoke heart [11]. Some phenolic compounds such as caffeoylquinic, quinic, and chlorogenic acids are presented in all waste parts but neochlorogenic and cryptochlorogenic acids were only found in bracts and receptacles [7,9,12].

Other vegetables as *Brassica oleracea* species whose inflorescence is consumed as broccoli and cauliflower contain high phenolic compounds concentrations in all aboveground parts, including leaves and stalks, which make up 70% of the aerial biomass [13,14]. Hydroxycinnamic acids are the main phenolic compounds found (more than 92% of total phenols) but neochlorogenic acids and chlorogenic acids are also highly found in these species [13,15,16]. Specifically, broccoli by-products have a high concentration of kaempferol, quercetin, and caffeic acid [17,18]. The phenol content varies according to the part of the plant, with a higher content of total phenols and specifically flavonoids in the leaves than in the florets, stalks, and cores [19,20] but also comparing different cultivars [19].

Other types of crops that contain a huge diversity of phenolics compounds are fruit trees such as *Citrus* sp. This genus includes orange, tangerine, lemon, and grapefruits, which are consumed as fresh fruit or processed into juice [5]. Millions of tons of Citrus wastes are generated annually, which can be a valuable source of polyphenols and flavonoids [21]. The by-products generated from citrus processing, including the peel (flavedo and albedo), pulp residue (rag), and seeds, make up over 50% of the fruit. These by-products are mainly rich in flavonoids [5]. Accordingly, the peels of citrus fruits, particularly oranges, have higher phenolic content compared to the edible portions, containing compounds like hesperidin. The citrus pomace water extracts also have significant phenolic and flavonoid content [22] with high content of hesperetin-7-O-rutinoside, quercetin, peonidin, and apigenin [21–24].

Grape (*Vitis vinifera* L.) is another fruit of great economic importance, being Europe the leading wine producer globally, with France, Italy, and Spain as the top countries. The winemaking process generates significant amounts of by-products such as vine shoots, grape stalks, wine lees, and grape pomace. In this way, grape pomace, which consists of peels, pulp, and seeds, accounts for 62% of the organic waste [5] is very rich in phenolic compounds, particularly quercetin [3,25]. But also, it has been described that grape pomace extraction showed high diversity of anthocyanins such as malvidin [25,26]. Additionally, grape by-products are also the best source of resveratrol, a stilbenoid type of natural phenol with great antioxidant characteristic [27]. In grape, the variety factor is very important as different grape varieties exhibit specific distributions of phenolic compounds [28] .

The cultivation and processing of tomato (*Solanum lycopersicum* L.) is also among the most waste-producing crops and with a higher content of phenolic compounds. Tomato waste residues include rotten ripe or defective tomatoes, stems, leaves, branches, and tomato fruit processing wastes such as pulp, seeds, and peels [5,29]. The main polyphenols found in tomato by-products are flavonoids, with

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naringenin and chrysin being the predominant compounds [15,30,31]. Tomato peels contain a higher concentration of phenolic compounds compared to seeds and pulp, with flavonols such as quercetin, naringenin, and rutin [6]. The phenolic content tends to increase during the stages of maturation, but genetic control and environmental factors also influence the accumulation of polyphenols [29]. Tomato pomace, which are the remaining solid waste from industry, has a lower content of phenolic compounds compared to other by-products as grape, but it still contains phenolic acids and flavonoids such as naringenin and naringenin chalcone [3].

In the case of onion (*Allium cepa* L.), the agroindustry generates a significant amount of waste, accounting for approximately 15% of total production [32]. The content and location of phenols in onions vary depending on factors such as the layer, color, and type of bulbs [33]. The main components of onion waste are the outer fleshy layers, top and bottom bulb parts including roots, onion skins produced during mechanical peeling, and undersized, or damaged onion bulbs [34]. Onion skins, outer fleshy scales, and internal scales are rich in phenolics, including flavonoids like quercetin and its derivatives. Additionally, onion skins contain other phenolic compounds, including p-OH-benzoic acid, protocatechuic acid, and vanillic acids. Specifically, quercetin-4-O-glucoside is the major compound found in both onion peels and skins [35–37].

In recent years, the cultivation of mushroom species on different substrates has been gaining importance. It was observed that this cultivation can generate by-products such as mycelia, stipes, caps, not commercial mushrooms, and spent mushroom substrate with a considerable content of phenolic compounds [4,38]. Mushrooms do not have the enzymes to synthesize flavonoids although they can absorb these compounds from the substrate or plants from which they form mycorrhizae [39]. The profile of phenolic compounds varies according to the species micorhizae but in general gallic acid is the most predominant in fermentates and dry powder produced from residues derived from the cultivation of various mushroom species together with chlorogenic, cinnamic, coumaric, and p-OH-benzoic acids [4,40–42]. However, the extraordinary composition of the plant material by-products should be considered as primary material. Therefore, harvest and storage should be carried out in the same way, or all the bioactive compounds will be lost.

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Table 1. Main phenolic compounds found in different crop by-products.

Species	Phenolic compounds	References
Artichoke	Apigenin, Caffeic acid, Caffeoylquinic acid, Chlorogenic acid, Coumaric acid, Cynarin, Ferulic acid, Luteolin Naringenin, Narirutin, Quinic acid	[7,9–11]
Broccoli	Caffeic acid, Chlorogenic acid, Coumaroylquinic acid, Ferulic acid, Kaempferol, Quercetin, Sinapic acid	[13,15,19,20]
Cauliflower	Caffeic acid, Coumaric acid, Ferulic acid, Kaempferol, Lutein, Quercetin, Sinapic acid	[16,43,44]
Citrus sp.	Apigenin, Benzoic acid, Caffeic acid, Caffeine, Caffeoylquinic acid, Caffeoyltartaric acid, Catechol, Catechin, Chlorogenic acid, Cinnamic acid, Cyanidin, Delphinidin, Dihydroxyflavone, Diosmin, Ellagic acid, Eriocitrin, Eriodictyol, Ferulic acid, Gallic acid, Gentisic acid, Hesperetin, Isorhamnetin, Isosakuranetin, Kaempferol, Luteolin, Malvidin, Myricetin, Naringenin, Naringin, Narirutin, Neoeriocitrin, Neohesperidin, p-OH-benzoic acid, Pelargonidin, Peonidin, Phloretin, Propylgallate, Quercetin, Resveratrol, Rosmarinic acid, Rutin, Scopoletin, Sinapic acid, Sinensetin, Syringic acid, Vanillin, Vanillic acid, Vitexin	[21–24,31,45–48]
Grape	Apigenin, Catechol, Catechin, Caftaric acid, Chlorogenic acid, Chrysoeriol, Cinnamic acid, Coumaric acid, Coutaric acid, Cyanidin, Delphinidin, Ellagic acid, Epicatechin, Eriodictyol, Ferulic acid, Gallic acid, Hesperidin, Hydroxybenzoic acid, Hyperoside, Isorhammnetin, Kaempferol, Luteolin, Malvidin, Morin, Myricetin, Naringenin, Peonidin, Petunidin, Procyanidin, Protocatechuic acid, Pyrogallol, Quercetin, Resveratrol, Rosmarinic acid, Rutin, Sinapaldehyde, Synergistic acid, Syringic acid, Vanillic acid, Ɛ-viniferin	[3,25,28,49–53]
Tomato	Apigenin, Caffeic acid, Catechin, Chloretic acid, Chlorogenic acid, Chrysin, Cinnamic acid, Coumaric acid, Eugenol, Gallic acid, Isoquercetin, Isorhamnetin, Kaempferol, Luteolin, Myricetin, Naringenin, p-OH-benzoic acid, Protocatechuic acid, Quercetin, Resveratrol, Rutin, Sinapic acid, Syringic acid, Vanillic acid	[3,15,25,30,31,54,55]
Onion	Coumaric acid, Ferulic acid, Isorhamnetin, Kaempferol, Myricetin, p-OH-benzoic acid, Protocatechuic acid, Quercetin, Vanillic acid, Vanillinic acid	[35,37]
Mushrooms	Caffeic acid, Catechin, Catechin gallate, Chlorogenic acid, Cinnamic acid, Coumaric acid, Ferulic acid, Gallic acid, Luteolin, Myricetin, Naringenin, p-OH-benzoic acid, Protocateic acid, Rutin, Syringic acid, Vanillic acid	[4,56–59]

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3. Extraction Processes and Inner Stability of Compounds

Conventional extraction including solid-liquid extraction (SLE) or soxhlet extraction, liquid-liquid extraction (LLE) and maceration are the main methods used for phenolic extraction that depend on type of sample (solid vs liquid) to extract and type of phenolic compound of interest (polar o non-polar). However, new methods have been also developed in order to fulfil the niche of the conventional methods misses or flaws. Although there are many of them, the more suitable for phenolic extraction is supercritical CO_2 extraction (SC-CO_2). Accordingly, the specific process used will provide different profile of phenolic compounds and should be chosen according to the higher concentration of actives need. We will review some of them that offer high feasibility with plant phenolic compounds.

Conventional extraction methods have long been used for the extraction of phenolic compounds from various plant sources. These methods include maceration, decoction, percolation, infusion, digestion, serial exhaustive extraction, and Soxhlet extraction [60]. But some of them are not recommended for phenolic extraction due to the degradation of the samples.

Maceration is a simple method that involves immersing plant material in an appropriate solvent (for polar or non-polar polyphenols) within a closed system and agitating it at room temperature [61]. Once the soaking process is complete, the solid plant material needs to be separated from the solvent, which can be achieved through filtration, decantation, or clarification methods [62]. However, despite its straightforward nature, maceration has some drawbacks. It can be time-consuming and requires a significant volume of solvent, leading to higher costs. Although maceration has been used for phenolic compounds extraction of artichoke heads [63,64]; *Citrus reticulata* [65]; citrus peel [66] and olive leaves [67], the yield is lower than other methods.

Percolation, closely resembling maceration, involves placing finely powdered samples within a sealed system, followed by the gradual introduction of solvent from the upper to the lower regions [68] .It should be noted that the extraction equipment is commonly integrated with filters that allow solvent passage. Nevertheless, percolation shares common challenges with maceration, including extended extraction times, significant solvent volumes, and considerations related to the solubility of polyphenols, sample size, and extraction duration. Modified applications of percolation have been explored, particularly in the context of artichoke extractions [69]. However, the method is seldom used in contemporary practice, although yield highly than maceration but lower that straightforward and higher-yield alternatives.

With *Soxhlet* extraction process, powdered samples are placed in nitrocellulose thimbles within an extraction chamber equipped with a reflux condenser, positioned above a collecting flask. The solvent in the heating bottle is vaporized, and the resulting vapor condenses, returning to the thimbles containing the sample. Excessive heating can potentially impact the extraction of thermolabile polyphenols [70,71]. Furthermore, Antony and Farid (2022) [70] claimed that more investigation is needed to understand the behavior of polyphenols during extraction at high temperatures. These methods involve using specific organic solvents at defined concentrations, including methanol, water, chloroform, n-hexane, propanol, ethyl acetate, and acetone, each with varying polarities that influence phytochemical extraction. The use of these solvents mix makes them suitable for enhancing extraction yields [72]. Therefore, although this soxhlet technique has been widely used for phenolics extraction, such as in broccoli plants [73,74], citrus [75], grape [76] and artichoke [77], the choose of right solvent for specific phenolic compounds should be determined since there is no universally best solvent mix.

Most laboratories prefer conventional extraction methods due to their affordability and simplicity. However, some innovative methods have emerged in recent years, including *supercritical CO_2 extraction* (SC-CO2) while originally tailored for non-polar compounds, SC-CO2 can be adapted for the extraction of polar compounds as well [78] which has been extensively used for the extraction of resveratrol from grape pomace. The most used solvent has been 5% ethanol at modified pressures of 100-400 bar and temperatures of 35-55 °C [79]. SC-CO_2 has also been optimized for extracting phenolic compounds from broccoli leaves, resulting in high extraction yields [80]. In the same way,

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microwave-assisted extraction (MAE) [81] used for artichoke [82] broccoli [73], citrus [83,84] and tomato [85]. Also, ultrasound-assisted extraction (UAE) [86] is commonly used for Artichoke [87–89], broccoli [90], tomato [15], grape [91]. Enzyme-Assisted Extraction (EAE) has garnered attention for its favorable impact on polyphenol extraction. Notably, studies have reported substantial polyphenol yields when employing cellucast®, pectinex®, and novoferm® enzymes as pretreatment agents during the extraction of polyphenols from grape waste [92]. Pressurized fluid extraction (PFE) is used for extracted anthocyanins from grape skins in which a solvent mixture of HCl, acetone, methanol, and water (0.1:40:40:20) was found the most effective [93].

These unconventional methods offer advantages such as reduced solvent usage, improved yields, fewer toxic residues, better reproducibility, and, in some cases, shorter extraction times. These methods can also be combined for enhanced extraction efficiency [94]. Therefore, parameters such as solvent type, solvent-to-sample ratio, extraction time, temperature, and pressure should be always characterized to enhance the extraction efficiency and yield of phenolic compounds from plant material. Therefore, while all of these extraction methods have the potential to yield high amounts of phenolic compounds, the actual yield mostly depends on the plant material. Hence, it is essential to optimize extraction conditions for each method to achieve the highest possible yield from a given sample. Additionally, a combination of different extraction techniques or the use of sequential extraction steps may be very useful to maximize the overall yield of phenolic compounds.

4. Cosmetic Formulation

Due to the high competition in the cosmetic market and the incessant demand for new and increasingly natural products, phenolic compounds have received special attention in recent years, as they offer numerous benefits for the skin and hair [95].

The concentrations of phenols in cosmetic products can vary widely depending on the type of phenolic compound, the product format, its specific function, and the regulations of the country where the product is marketed. In the European Union (EU), a high number of cosmetics containing phenols in their formulations are commercially available (Figure 1). However, some of these formulations are under patent, making it impossible to know their exact composition and concentrations.

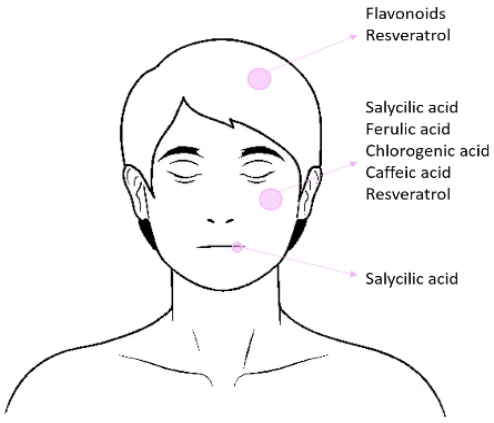

Figure 1. Phenolic compounds present in the formulations of products marketed in the EU.

When formulating, particularly with phenolic compounds, there are several physicochemical characteristics that must be considered. Emulsified systems, also known as emulsions, are the most common and widely known formulation in the cosmetic industry [96]. They can be defined as the mixture of two immiscible liquids, such as oil and water, which remain stable due to the presence of an emulsifying agent. Nevertheless, detrimental phenomena, like lipid oxidation, might occur at the interphase of the emulsion. This is usually mainly provoked by the presence of water-soluble pro-oxidants and the degree of unsaturation of the lipid phase [97]. In this way, phenolic compounds (e.g. flavonols, caffeic acid) are a great option to include in these formulas, since their action as antioxidants can prevent the lipid oxidation and both can act as a bioactive. However, the optimal

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concentration of phenolic compounds present in the formula can be affected by their oxidation and subsequent deactivation. Consequently, there are different parameters that must be considered in order to formulate with phenolic compounds, in order to achieve a stable emulsion with an optimal concentration of bioactives that serve to both purposes: increase the preservation of the formula and contribute to the effectiveness of the cosmetic.

Physicochemical properties of the molecules, such as their polarity, can directly affect diverse properties like solubility, reactivity, and their capacity to react with other compounds or molecules. The polarity is determined by the oil-water partition coefficient ($logP_W^O$), which can be defined as the logarithm of the ratio of phenolic compound concentration present in the oil phase to the water phase without the presence of emulsifier. Thus, a negative partition coefficient value corresponds with a higher presence of the phenolic compound in the water part of the system, meanwhile a positive value indicates a higher proportion of it in the oil phase [98].

In an emulsion system there are three distinct phases: the aqueous phase, the oil phase and the oil-water interface (Figure 2). The distribution of the phenolic compounds in these phases will depend on their nature. However, it is difficult to define the exact distribution of a phenolic compound in the different phases of the emulsion system based only on the polarity. Since the oil-water interface is a narrow and anisotropic region surrounding the emulsion droplets, its structural composition is directly influenced by the type and concentration of the molecules present in it. In this way, also the thermodynamic features of the phenolic compounds must also be considered in order to comprehend their adsorption to the surface of the droplet [99].

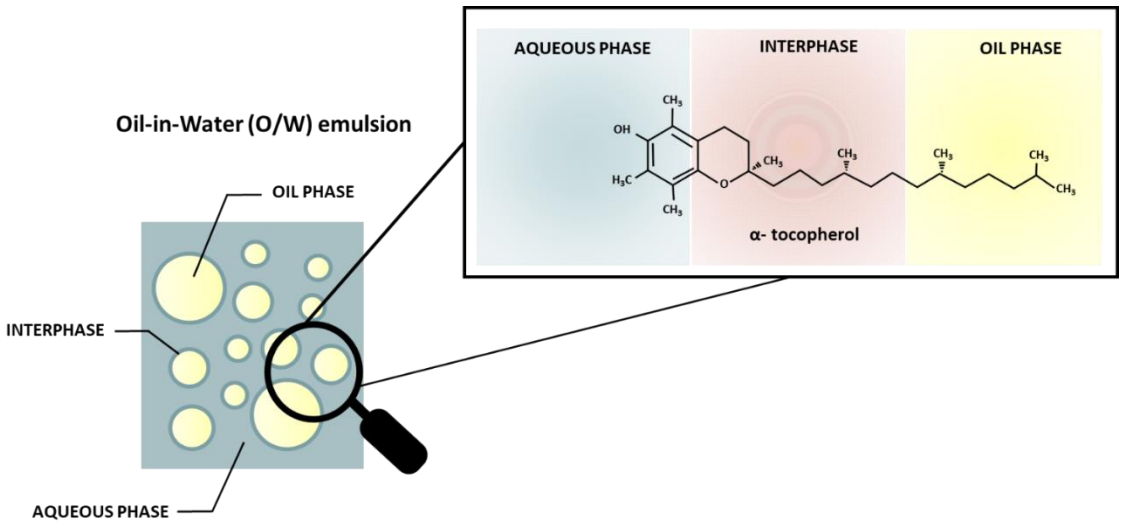

Figure 2. Scheme of the different phases present in an oil-in-water emulsion and an example of a phenolic molecule distribution.

4.1. Polar Phenolic Compounds

Catechin. This polyphenolic compound is commonly present in extracts derived from green tea, berries, cocoa or grape seeds. Also known as flav-3-ol, catechin has demonstrated to be competitively adsorbed in the oil-water interface, decreasing the interfacial tension in a concentration-dependent way when introduced in an olive oil O/W emulsion. This characteristic is due to the presence of a central heterocyclic oxygenated ring and two benzene rings [100]. In addition, it has been reported that this structure grants catechin a high ability to interact with the emulsifiers through hydrophobic, hydrophilic or covalent interactions, which increases its ability of stabilize the oil-water interface of the emulsion and thus, giving a highly stable cosmetic emulsion [101].

Caffeic acid. 3,4-dihydroxycinnamic acid, also known as caffeic acid, is mainly found in ingredients derived from coffee, olive oil and wine, among other vegetable sources. Resonance and conjugation effects occur in the caffeic acid molecule due to the presence of the CH=CH bridge between the carboxyl group and the aromatic ring [102]. Thus, its antioxidative effect in oil-in-water

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emulsions is directly correlated with its ability to delay the initiation and propagation stages of lipid oxidation by donating an H atom to free radicals o by acting as a metal chelator [103].

Caffeic acid and also chlorogenic acid are two hydroxycinnamic acids recognized for their potent antioxidant capabilities, which grant them antibacterial and antiviral properties. Moreover, they enhance skin texture by illuminating it and combatting signs of aging. They have the ability to increase collagen production and protect the epidermis from UV rays [104]. Both of these acids can be found in concentrated serums from various brands such as The Ordinary, SkinBetter, and Skinphysics.

Gallic acid, or 3,4,5-trihydroxybenzoic acid, has been included in different formulas thanks to its capability of accepting electrons and holding charges due to the presence of hydroxyl groups in an ortho-position. This, gives the molecule a coplanar and bent configuration that allows its antioxidant activity [105]. In addition, gallic acid is mainly found in red grapes, berries, diverse nuts and tea-derived extracts. In an emulsifying system, gallic acid has demonstrated its ability to increase the interfacial area of an olive oil-in-water emulsion in a dose-dependent trend [106]. This highly contributed to decreasing the emulsion, since it is a negative charged molecule, preventing the droplets from interacting and precipitating.

Rosmarinic acid is a polyphenol mainly derived from rosemary, sages and thymes. This molecule consists of two aromatic rings, each bearing a hydroxyl group in the ortho-positions. These groups have demonstrated the potential to donate hydrogen atoms to lipid free radicals. In this way, rosmarinic acid shows a high ability of inhibiting the formation of volatiles and hydroxoperoxides. Also, rosmarinic acid has shown a high capability to quench superoxide anion radicals present in oil-in-water emulsions [107]. Nevertheless, it has been demonstrated that rosmarinic acid antioxidant properties are strongly affected by pH, decreasing from pH 5 to pH 7 [108].

Hydroxytyrosol is one of the most popular olive-based phenolic compounds, mainly due to its ability of donating a hydrogen or electron to free radicals. Furthermore, its high bioavailability allows its use in cosmetic formulation with less toxicity. Its antioxidant mechanisms in an oil-in-water emulsion is mainly related to the donation of the H-atom present in its three hydroxyl groups attached to the aromatic ring in an ortho position. However, the pH of the formula has been highly related with its action as a prooxidant as well as the presence of ferric ions, mainly working as an antioxidant around pH 7.4. In addition, its introduction in emulsified system is highly conditioned by the processing conditions. In this way, hydroxytyrosol also occurs forming covalent and noncovalent complexes [109].

4.2. Non-Polar Phenolic Compounds

***α**-tocopherol*, also known as a part of the vitamin E group, are mainly found in sunflower and olive oils. This molecule has a chromanol ring linked to a –OH ring that is the mainly responsible of its antioxidant activity, thanks to the donation of the H-atom. Although α-tocopherol possesses a high reduction potential, it might also act as a prooxidant, depending on its concentration and the pH and temperature of the final formula [110,111]. In addition, α-tocopherol's hydrophobicity is directly related with its phytyl moiety, which conditions this molecule for the addition of a carrier that facilitates its incorporation in an oil-in-water emulsion [112]. For example, α-tocopherol within chitosan and collagen carriers used in corn oil-water emulsions stabilized by Tween 20 demonstrated a greater antioxidant efficacy at 60°C [113].

Curcumin is mainly obtained from *Curcuma longa*. This lipophilic polyphenol primarily exerts its activity by a mechanism of cation-binding, thanks to three chelation sites: a β-diketone moiety and two hydroxyl groups present at both ends of the molecule [110]. Depending on pH, this molecule has shown two different mechanisms of action: between pH 3 to 7, its action mainly resides in the H-atom transfer from the heptadienone moiety, however above pH 8, it turns into an electron-donating mechanism [114]. Additionally, curcumin has demonstrated a low water solubility, being nanoeumlsion-based system an efficient option for releasing curcumin into the oil-water interface [115].

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Quercetin is mainly present in extracts derived from black tea, apples, berries and onions, and contains a 3-hydroxyflavone backbone with five hydroxyl groups located in position 3-4 and 3-5-7. Thanks to this structure, it provides three complexing sites to metal cations, acting as a strong chelating agent. Furthermore, quercetin possesses a poised equilibrium due to the presence of the catechol structure (3'-4'dihydroxy in the B ring) and the 3,5-OH groups present in the C ring. This enables this molecule to strike a balance between associating with the lipid droplet surface to inhibit lipid oxidation and engaging with ferric ions (Fe^{3+}) present within the aqueous phase [116].

Salicylic acid, also known as 2-hydroxybenzoic acid or orthohydrobenzoic acid, is widely used in cosmetic formulation. The main sources of natural origin for this compound and salicylate derivatives are birch, poplar and willow bark [117]. Salicylic acid (SA) is a lipid-soluble agent and thus, highly compatible with epidermal lipids and sebaceous accumulations in follicles [118]. It is recommended for individuals with acne-prone skin due to its ability to regulate sebum secretion. Salicylic acid has the capacity to exfoliate the skin, as well as cleanse and reduce pore size [119]. The level of exfoliation is directly proportional to its concentration in the product, and a typical cosmetic usage involves a concentration of 2% [120]. Its diffusion from O/W emulsion has been demonstrated to be higher at pH 4.6 [121]. Furthermore, it has been mainly used as an exfoliating ingredient thanks to its ability of removing intercellular lipids and, due to the presence of the organic ring, its action on desmosomes, provoking the detachment of the statum corneun cells [121,122]. Combrinck et al. (2014) [123] studied the diffusion of salicylic acid from the oil phase in an oil/water emulsion, obtaining a decrease in release of salicylic acid with an increase in the pH. In this way, demonstrating that its crucial for SA the pH of the selected formulation.

Ferulic acid, also known as 4-hydroxy-methoxycinnamic acid, is a derivative of cinnamic acid that presents an elevated antioxidant capacity due to the presence of the phenolic ring and the unsaturated side chain, which can result into a resonance stabilized phenoxy radical [124]. Ferulic acid can be mainly found in extracts derived from some cereals, flaxseeds and vegetables like pineapple, bananas, spinach, beetroot, artichokes and coffee beans [125]. In addition, ferulic acid has shown a great stability in both oil-in-water and water-in-oil emulsion, achieving a great permeation coefficient under diverse formulas [126]. However, it has been demonstrated that ferulic acid showed no antioxidant activity in O/W emulsions with a high proportion in ω-3 fatty acids stabilized with whey proteins [127]. According to partition coefficient of ferulic acid, in a system of fish oil-water, it has been observed that its dissociated form is highly hydrophilic but its undissociated form presents a higher hydrophobicity, being a relevant fact to consider when formulating [128].

Resveratrol is a novel ingredient in cosmetics owing to its anti-aging activity. This compound has the ability to penetrate the skin barrier and stimulate fibroblast proliferation, while also increasing collagen III concentration. Like other phenols, its antioxidant capacity enables it to shield the skin from UV radiation and mitigate the process of skin photoaging. In such products, it is often present at concentrations of around 5%, either as a pure ingredient or as part of a grape extract [129].

5. *In Vitro* Effects

This section intends to summarise and analyse several *in vitro* assays carried out to explore the cosmetic effects of phenolic compounds. The initial phase entails establishing the effective concentration (EC50), which represents the quantity of the compound required to produce a 50% response. Thereafter, assays are performed to evaluate different features as the antioxidant effect, the anti-inflammatory capacity, or the antimicrobial properties [130].

5.1. Antioxidant Effect

Oxidative stress is a condition that affects the skin and can be caused by internal and external factors. Aging and exposure to solar radiation (UV-A and UV-B) are notable factors. This kind of stress primarily produces reactive oxygen species (ROS) that affect cells at various levels. Therefore, plant extracts rich in phenolic compounds have been used to prevent or treat the oxidative stress effects. Assays to evaluate the antioxidant potential are based on determining the ability to neutralize free radicals and reduce oxidative stress [131]. This is commonly done through the use of various

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spectrophotometric methods, including the DPPH assay (1,1-diphenyl-2-picrylhydrazyl), FRAP, and ORAC.

Artichoke extracts, as stated above, are rich in different polyphenols, including hydroxycinnamic acids and flavonoids. Chlorogenic acid, a hydroxycinnamic acid, acts as a free radical scavenger and a UV protector [132]. Studies conducted using extracts derived from artichoke have yielded noteworthy findings. Ethanol-based extracts from artichoke heads have been shown to enhance the functions of endothelial cells whilst also increasing the expression of genes responsible for oxidative stress protection and the formation of tight junctions, which play a crucial role in maintaining the structure of skin cells. Additionally, they affect other genes such as VEGF, ET-1, or eNOS, which are involved in angiogenesis and the elevation of capillary permeability – factors affected during ageing [64]. Furthermore, three types of artichoke leaf extract (infusion, decoction, and hydroalcoholic) have exhibited notable scavenging capacity [133] . In addition, artichoke extract also contains compounds that act as *in vitro* solar protection factor (SPF), including flavonoids [134].

Citrus species possess multiple health-promoting properties due to the presence of different bioactive compounds, such as phenolics [135]. Concerning skincare, the ability to protect and prevent UV-induced damage of extracts from red orange (*Citrus sinensis* L. *Osbeck*), have been examined for their ability to protect and prevent UV-induced damage in fibroblast and keratinocytes. It has been reported that they prevent oxidative stress by averting DNA damage and extracellular matrix degradation [136]. Extracts of *Citrus lemon* peel have also been tested and resulting in protect keratinocytes cells against oxidative stress. This is achieved through the regulation of the Nrf2/HO-1 signalling pathway by improving antioxidant enzymes such as SOD, GSH, and CAT. Compounds identified in the extract, such as gallic acid, catechin, or caffeic acid, were attributed to this effect [137]. The Brassica genus, specifically broccoli (*B. oleracea* var. *italica*) is widely known due to their beneficial properties. Extracts enriched in phenolic compounds from various broccoli by-product, such as leaves, exhibit high antioxidant activity. This is attributed to a variety of compounds, including kaempferol [138], whose action mechanism has been partially elucidated and is linked to the ROS/JNK/NF-κB signalling pathway, demonstrating its potential as a suitable cosmetic ingredient against the skin dermal fibroblastic inflammation and oxidative damage [139]. These properties have been previously described in various plant-derived extracts abundant in phenolic compounds. For example, *Aloe vera* by-products (skin) exhibit *in vitro* free radical scavenging activity due to their phytochemicals and antioxidants [140]. By-products produced from olive oil production are rich in hydroxytyrosol, resulting in a reduction in the formation of ROS, malondialdehyde (MDA), activity of glutathione-S-transferase (GST), and superoxide dismutase (SOD). Additionally, an increase in microRNAs involved in both redox status balance and skin regeneration has been observed as a result of their use [141]. The wine production industry also generates significant by-products. Grape-derived by-products, with their high content of phenolics, have been tested *in vitro* for their antioxidant activity and potential use in the cosmetic industry [142–144]. Similarly, the berry industry generates agricultural waste, with leaves being a by-product that have been used to made extracts and prove their significant ability to remove free radicals in keratinocytes and fibroblasts *in vitro* [145]. On the other hand, coffee silverskin, the predominant solid by-product from the coffee roasting process, was used to obtain enriched phenolic extracts that shown an antioxidant activity ranged from 206 to 287 μmol Trolox equivalent/g and 95–217 μmol Fe^{2+}/g by DPPH and FRAP methods. Besides, tested concentrations were no cytotoxic on keratinocytes and fibroblasts [146]. Similarly, extracts obtained from pomegranate were tested on human keratinocytes and showed no toxicity at any of the concentrations tested [147]. Another specific mode of action for these types of extract is to enhance the synthesis of collagen and elastin, crucial proteins for skin firmness and elasticity, which are affected by oxidative stress caused by UV radiation and these can be measured by using western blot or ELISA techniques specific to these proteins. The degradation of both collagen and elastin is crucial to the aging process. Therefore, addressing at this level is also important, and it has been shown that phenolic compounds have this effect as well [148].

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5.2. Anti-Inflammatory Effects

Similar to the above description regarding antioxidant activity, a multitude of *in vitro* assays can be found to study the anti-inflammatory effects of various plant extracts rich in antioxidant compounds. The anti-inflammatory capacity of the compounds is assessed by measuring the inhibition of inflammatory mediator production through techniques like ELISA or quantitative PCR. Additionally, oxidative stress and inflammation are physiologically interconnected, so most tests encompass a dual approach to assess both activities, as they will be related to each other. In this context, research can be found with extracts from different sources: citrus peels, which are able to inhibit the production of pro-inflammatory cytokines (TNF-α, IL-6, IL-1β) [149], extracts from artichoke that are able to inhibit pro-inflammatory mediators (IL-6 and monocyte chemoattractant protein 1) [150], formulations based on red grape pomace extract that decreased the release of the pro-inflammatory cytokine IL-8 [151], aqueous olive extracts that diminished secretion of pro-inflammatory cytokines (IL-1α, IL-1β, IL-6, IL-12, TNF-α), chemokines (CXCL10/IP-10, CCL2/MCP-1), and reduced the expression of genes related to inflammation and oxidative stress, including inducible nitric oxide synthase (iNOS), IL-1α, CXCL10/IP-10, MIP-1β, or matrix metalloproteinase-9 [152], and formulation based on cell membrane component from broccoli leaf that decreased the production of pro-inflammatory cytokines (IL-1β, IL-6, and TNF-α) in human macrophages [153].

5.3. Antimicrobial Effect

The antimicrobial capacity of phenolic-rich extracts has been extensively tested in various fields. Moreover, assessing the antimicrobial effect involves conducting *in vitro* assays against skin-associated pathogenic microorganisms, evaluating the inhibitory effect on bacterial and fungal growth to understand the ability of the compounds to safeguard the skin against infections. When focusing on cosmetics, it becomes evident that multiple types of infections can affect the skin, leading to dermocosmetic issues such as acne, a highly prevalent dermatological condition worldwide. Among the pivotal factors contributing to the development of this condition is the bacterial colonization by bacteria of the genus *Propionibacterium* and *Staphylococcus*, which subsequently triggers an inflammatory process [154]. Hence, phenolic compounds demonstrate efficacy not solely due to their antimicrobial capabilities, which will be elucidated below, but also owing to their previously mentioned anti-inflammatory attributes. Their antimicrobial potency arises from their capacity to inhibit the growth and proliferation of pathogenic microorganisms, which is of paramount importance in combating skin infections. For instance, *in vitro* studies have demonstrated the inhibitory effects of plant extracts rich in phenolic compounds, such as green tea extract (*Camellia sinensis*), against *P. acnes, P. granulosum, S. aureus, or S. epidermidis*— microorganism implicated in the development of acne. The results of this study indicated a remarkable inhibition of 98 % of bacterial growth at a concentration of 400 μg gallic acid equivalents mL^{-1} of the green tea extract [155]. Similar outcomes were achieved with an extract obtained from coffee silverskin, which exhibited significant antimicrobial activity against *S. aureus* and *S. epidermidis*, without cytotoxicity in skin cells such as fibroblast and keratinocytes [146]. In the context of acne, various types of cinnamon extract have demonstrated activity against two bacteria known to cause acne, *P. acnes* and *S. epidermidis*. In this study, the authors attributed the antibacterial activity to phenolic compounds such as cinnamaldehyde and eugenol [156,157]. Pomegranate is another popular source of phenolic compounds. Pomegranate extract derived from peels has shown effectiveness in inhibiting several dermatophyte fungi, including *Trichophyton rubrum*, *Trichophyton mentagrophytes*, and *Microsporum canis* [158]. Furthermore, significant antibacterial activity has been observed against *E. coli, S. aureus, and Listeria* [159]. Due to this potent antibacterial activity, coupled with its antioxidant activity primarily attributed to phenolic compounds - specifically punicalagin - pomegranate by-product extracts are being considered for various cosmetic applications.

Phenolic compounds, which are abundant in various plant sources, offer a multifaceted range of benefits for skin health. Their antioxidant, anti-inflammatory, and antimicrobial properties make them promising candidates for cosmetic applications. Further investigation into their mechanisms of

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action and clinical studies will likely unveil even more opportunities for these compounds in the skincare industry.

6. *In Vivo* Effects

Although *in vitro* studies demonstrated the significant potential of plant extracts enriched in phenolic compounds for their application in cosmetic formulations, it is essential to ensure the reproducibility and non-toxicity of these results for users. In this way, as the use of natural ingredients has been associated with some adverse cases of skin allergies, conducting *in vivo* studies becomes still necessary to guarantee and evaluate their efficacy, determine the appropriate dosage, and address any potential toxicological concerns [160–162]. Nevertheless, the gradual transition to *in vivo* testing from quantitative *in vitro* and computational (*in silico*) approaches is a priority endorsed by REACH (Registration, Evaluation, Authorisation, and Restriction of Chemicals), in line with the 3Rs principle and the use of alternative methods to minimize animal testing in current regulatory practices, and considering that the Cosmetic Regulation (EC 1223/2009) bans *in vivo* animal testing [162,163]. Therefore, the advantageous cosmetics properties shown *in vitro* must be tested *in vivo* to confirm them [164].

While many plants enriched in phenolics have had their extracts characterized, only a few have been tested *in vivo* to determine their potential in cosmetics or pharmacosmetics in addition to *in vitro* studies. However, the ones that have been studied show promising results in these areas (Table 2). But no studies have been performed to conferring to a concrete phenolic a specific skin activity. Therefore, the activity has been related to an extract with a complex chemical composition. For example, extracts rich in caffeic acid, caffeoylquinic acids, quercetin, etc., including anthocyanins exhibited *anti-melanogenesis* activity by powerfully inhibiting tyrosinase (IC50 = 12,48) and melanin synthesis *in vitro* [165]. Also, no irritation has been shown when applied in guinea pigs (n=33) and in female human skin (n=50) during 24 hours. Additionally, they are attributed to skin whitening, moisturizing, and erythema-decreasing activities when applied as a 4% oil-in-water cream containing 4% concentrated ethanolic extract on male human face during 8 weeks (n=11), by inhibiting melanin production (measured with a mexameter), retain water content (measured by corneometry), and restore the lipid barrier's ability to attract, hold, and redistribute water, thereby maintaining skin integrity and appearance [166].

Also, high phenolic content, including chlorogenic acid, caffeic acid, ferulic acid, and flavonoids, among others as coffee extract has recently emerged as a potential extract in natural dermocosmetics. Certain fractions enriched in phenolic compounds, such as alpha-tocopherol, have been tested through topical application (5 mg/cm^2) in female hairless mice (n=N.I. (not indicated)) 24 hours after UV irradiation, and have shown promising dermocosmetic effects, acting as antioxidants and providing photoprotective activities, which were performed by reducing the formation of epidermal lipid hydroperoxides, halving the glutathione content [167–169]. In the same way, when formulating a product with an extract rich in caffeic acid, acid, chlorogenic acid, coumaric acid, cynarin, ferulic acid, luteolin naringenin, narirutin, quinic acid as provided by artichoke, at a concentration of 0,002%, this extract has been shown to enhance skin roughness and elasticity. Over the course of a month-long application on female human with sagging facial skin (n=20), it demonstrates remarkable antioxidant, anti-inflammatory, and anti-aging properties, as it improves the wrinkle depth and skin elasticity properties. Furthermore, it acts as a protective agent for endothelial and lymphatic cells while also inhibiting vascular aging processes [64].

Extracts rich in caffeic acid, chlorogenic acid, cinnamic acid, coumaric acid, gallic acid, kaempferol and sinapic acid as contained in tomato resulted of pharmacosmetics interest, with optimal *in vivo* results, as *anti-inflammatory and anti-allergy activities*, in intravenous and nutraceutical studies, due to their great phenolics and carotenoids content [170]. For example, a 7% cream-based aqueous extract exhibited softener and moisturizing effects on human arm skin (n=40) 48 hours after the application, and on feet skin 24 hours after the application, showing promise in the emerging field of tomato dermocosmetics [171]. However, further investigations are necessary to explore the molecular antioxidant mechanisms or determine the preservation of these extracts as dermocosmetic

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formulations, given that the majority of investigations are orientated to gastric or medical treatments [172] .

Extracts rich in phenolics like flavonoids (quercetin), phenolics acids (hydroxybenzoic and hydroxycinnamic acids) and stilbenes as those contained in grape [173,174] emerged as one of the most extensively studied extracts in this area. In fact, there is a substantial research about formulations where grape (*V. vinifera)* phenolics are identified as potential active ingredients in cosmetic. Some studies demonstrate a *sunscreen protective* effect of this extract in both mice and human, thereby enhancing the value of cosmetic formulations. Before a UV-B radiation, a hydroethanolic extract prevents radiation damage by reducing levels of pro-inflammatory cytokines and sunburn cells, 24 hours after a single application in female hairless mice (n=40). These results respond to a significant decrease in pro-inflammatory cytokines level and antioxidant activity [173]. Furthermore, a grape 10% extract formulated in an oil-in-water emulsion with UV filters like butylmethoxydibenzoyl methane was tested on human (n=60) for 6 weeks. It presented significant photoprotective effectiveness by reducing 21% erythema formation after UV exposure compared to a sunscreen formulation alone [175]. Other studies in human reveal the antioxidant properties of grape extract formulation which improved various parameters, including radiant glow, smoothness, hydration, texture, and softness, primarily due to a decrease in reactive oxygen species (ROS) in the stratum corneum of photoaged skin (through a radical scavenging mechanism) after 4 weeks of twice daily application in female human forearm (n=60) [176]. Notably, the Muscat Hamburg' variety has demonstrated great potential in improving skin elasticity, and inhibiting erythema and hyper-pigmentation. This effect was observed when formulated as a 2% water-in-oil emulsion and tested on male human cheeks (n=110) over an 8-week period during winter. The effects are attributed to the tyrosinase-inhibitory activity of resveratrol (one of the most characterized and utilized stilbenes in cosmetology) and the enzymatic-inhibitory activity (acting as an anti-collagenase) of grape phenols, which prevent skin aging and deterioration [129,177] . In fact, an specific trans-resveratrol enriched extract from grapes, formulated as a 0,1% water-in-oil cream, reveals significant anti-aging effects and improvements in skin parameters (measured by colorimetry, elastometry, and corneometry) when applied during a month to skin-aged female human (n=8). The results were further enhanced when formulated with β-cyclodextrin, which increases the efficacy of resveratrol action [129,178].

Flavonones and phenolic acids as chlorogenic acid, cinnamic acid, ellagic acid, hesperidin, kaempferol, luteolin, naringenin, naringin, narirutin, and quercetin, mainly located in the peels of citrus fruits also represent innovative candidates in this field. These compounds have been extensively investigated in the field of biomedicine [179]. However, despite numerous *in vitro* findings suggesting beneficial cosmetic effects of phenolic compounds obtained from citrus, particularly in pharmacosmetics, comprehensive *in vivo* studies are lacking [180]. These extracts, including essential oils, have been evaluated for their *anti-inflammatory effects* [181,182]. Citrus extract showed an effective counteracting activity against the effects of UV exposure and photo-aging, improving skin parameters such as elasticity or moisturizing and decreasing lipid peroxidation and erythema generation [183]. A 3% mandarin ethanolic extract exhibits anti-inflammatory properties when applied for 36 days in an atopic dermatitis female hairless mouse model. This application led to a reduction in redness, hyperkeratosis, and wrinkles, showcasing its potential utility in anti-atopic formulations [184]. All these effects could be attributed to phenolic compounds such as naringenin and hesperidin since some *in vivo* studies using these individual compounds have demonstrated photoprotective properties when they deeply penetrate the skin, as observed in tests on humans after UV-inducing erythema [185,186].

The phenolic extracts with high content in chlorogenic acid, caffeic acid, coumaric acid, cerulic acid, kaempferol, quercetin, sinapic acid as obtained from brassicas have been investigated *in vitro*, but the *in vivo* mechanisms when they are included in cosmetic formulation have low studied [187–189]. In this way, extracts from *Brassica oleracea* var. *capitata* f. *rubra* (red cabbage) when formulated as an ethosomal gel (2% Carbopol gel) have demonstrated significant *antioxidant activity* with improvements in smoothness, reduced wrinkles, minimized facial pore size, enhanced skin hydration (measured by corneometry), increased elasticity, regulated sebum production, decreased erythema,

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and balanced melanin levels; observed and applied to female human cheeks [190]. These findings led to propose red cabagge extract as potentially active in dermatitis or acne vulgaris [191]. Furthermore, chlorogenic and quercetin-enriched ethanolic extract obtained from *Brassica nigra* (black mustard) has demonstrated significant *anti-inflammatory* activity. However, specific dermocosmetic by topic administration tests have not been conducted either, in chlorogenic or quercetin enriched extract [192]. Collectively, these results indicate promising potential for formulating dermocosmetics based on brassicas. Nonetheless, comprehensive *in vivo* investigations including topical tests are required to fully understand and harness their benefits.

Also, the vegetal extracts rich in coumaric acid, ferulic acid, vanillic acid, quercetin, from plants such as *Allium cepa* (onion), *Allium sativa* (garlic) or rich in caffeic acid, chlorogenic acid, cinnamic acid, coumaric acid, cerulic acid, gallic acid, vanillic acid, luteolin, myricetin, naringenin, catechin, and rutin, form *Agaricus bisporus* (mushroom), presented high antioxidant effect by radical scavenger or lipid peroxidation inhibition mechanisms showing moisturizing, anti-inflammatory effect. However, again these extracts have not been tested *in vivo* [193–196]

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Table 2. *In vivo* studies or tests summary related with dermocosmetics of plant species enriched in phenolics.

Plant specie	Formulation	Cohort	*In vivo* results	References
Brassica oleracea var. *Capitata* f. *rubra* (red cabbage)	Ethosomal Carbopol 2% gel	Female human	Strong antioxidant activity with remarkable dermocosmetic benefits for skin.	[191]
Centella asiatica	Emulsion and hidrogel (5% extract)	Human	Moisturizing and anti-inflammatory activities.	[129]
Citrus x sinensis (red orange)	Aqueous/Aqueous-ethanolic solution extract	Healthy human with UVB-induced skin erythema	Antioxidant by radical scavenger activity: skin photoprotection	[186]
	ROC™	Human forearm	Photoprotective, anti-erythematic and antiaging activitiea	[197]
Citrus unshiu (mandarin)	Ethanolic extract	Female SKH1-hairless mice.	Anti-inflammatory activity, useful as an anti-atopic agent.	[184]
Coffea arabica (coffee)	Alpha-tocopherol extract (5 mg/cm^2).	Female hairless mice	Antioxidant and photo-protective activities	[198]
Cynara cardunculus var. *Scolymus* (artichoke)	Ethanolic extract formulated in cream (0,002%)	Female human with sagging face	Improvement of endothelial cells integrity, by enhancement of skin roughness and elasticity	[64]
Diospyros kaki (persimmon)	Emulgel	Human	Anti-aging activity.	[199]
Morus alba (mulberry)	Oil/water emulsion with 4% ethanolic extract.	Human	Whitening, antierythemic and moisturizing activities.	[166]
Moringa (moringa)	Cream (14% paraffin oil) formulation	Male human	Moisturizing activity.	[200]
Solanum lycopersicum (tomato)	Glycerinated formulation (3%)	Human	Moisturizing activity.	[171]

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Vitis vinífera (grape)	Hydroethanolic extract (4 mg/40 µl/cm²)	SKH-1 hairless mice.	Photoprotective activity (against UV-B skin damage)	[173]
	Oil-in-water solution (10%)	Healthy human	Photoprotective activity, synergic with sunscreen chemicals formulation Antioxidant and anti-photoaging activities.	[175] [176]
	Sarmentine (1%) cream	Human	Anti-aging, moisturizing and skin whitening activities	[177]
	β-ciclodextrine formulated with solution (0,1%)	Human	Anti-aging activity	[178]

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7. Concluding Remarks

Phenolic compounds that are part of the secondary metabolism in plant tissues are getting considerable attention for their potent antioxidant and anti-inflammatory, which give anti-ageing, photoprotective, and antimicrobial properties in cosmetic products. Therefore, this could be a high value use for several worldwide produced by-products. However, as it has been reviewed in this work, there are some issues, form the harvest to the *in vivo* assays, that must be considered to reach an effective cosmetic formula. At first instance, it should bear in mind that plant material by-products should be considered as primary material and the chemical composition should be maintained as material for food. Therefore, harvest and storage should be carried out in the same way or all the bioactive compounds will be lost. Secondly, the extraction process (technology, solvent, pressures, time, etc) should be carefully chosen according to the specific phenolic compounds of interest. It is at this point where we found more lack of knowledge. The actions of phenolic compounds on skin could be summarized into antioxidant, anti-inflamatory and antimicrobial, which has been extensively studied *in vitro*. The strategies to undertake *in vitro* assays serve as a crucial tool in elucidating the properties and *in vivo* mechanisms of action of these compounds, but the in vivo studies are very scarce and need to be implemented. Therefore, the fact that plant phenolics may be efficient in the treatment of both serious life-threatening dermal diseases and minor skin problems is of high value due to the natural source of these compounds. In addition, the recovery of these compounds have a positive impact on mitigating climate change due to the circular economy. Furthermore, further investigation of the innate qualities and remarkable efficacy of crop by-products phenolic compounds offer promising prospects for the development of innovative topical formulations and dressings that could potentially replace existing therapeutic applications.

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