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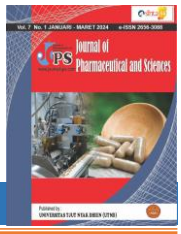

Rosemary (*Rosmarinus officinalis*) Phytochemicals as Prevention of Collagen Degradation and Wrinkle Formation: a Literature Review

Fitokimia Rosemari (*Rosmarinus officinalis*) untuk Mencegah Degradasi Kolagen dan Pembentukan Kerutan: sebuah Tinjauan Pustaka

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Abstract
Skin aging is characterized by progressive structural and functional changes in the skin, with wrinkle formation being one of the most visible manifestations. Aging disrupt the balance between collagen synthesis and degradation, leading to fragmentation of collagen fibers and loss of skin elasticity. Natural phytochemicals have gained increasing attention as potential agents for preventing or delaying skin aging due to their antioxidant and anti-inflammatory properties. Rosemary (*Rosmarinus officinalis*) contains a variety of bioactive compounds with potential dermatological benefits. Major phytochemicals identified in rosemary include phenolic acids such as rosmarinic acid, diterpenes such as carnosic acid and carnosol, as well as flavonoids and volatile terpenoids. These compounds have demonstrated strong antioxidant activity and the ability to modulate molecular pathways associated with skin aging. Evidence from in vitro studies suggests that rosemary phytochemicals can reduce reactive oxygen species (ROS) production, suppress inflammatory signaling pathways, and inhibit the expression of MMPs involved in collagen degradation. Emerging clinical evidence, particularly from oral supplementation studies, also suggests improvements in skin elasticity, wrinkle depth, and oxidative stress biomarkers, supporting the translational potential of rosemary phytochemicals in human skin. Available evidence supports the potential application of rosemary-derived compounds in dermatological and cosmeceutical formulations aimed at preventing collagen degradation and wrinkle formation. This literature review summarizes current evidence on the phytochemical composition of rosemary and the molecular mechanisms through which its bioactive compounds may contribute to the prevention of skin aging.

***Keywords*: Aging, Antioxidant, Collagen, Rosmarinus officinalis.**

Abstrak
Penuaan kulit ditandai oleh perubahan struktural dan fungsional yang berlangsung secara progresif, dengan pembentukan kerutan sebagai salah satu manifestasi yang paling terlihat. Penuaan mengganggu keseimbangan antara sintesis dan degradasi kolagen, yang menyebabkan fragmentasi serat kolagen dan hilangnya elastisitas kulit. Senyawa fitokimia alami semakin mendapat perhatian sebagai agen potensial untuk mencegah atau menunda penuaan kulit karena sifat antioksidan dan antiinflamasinya. Rosemari (*Rosmarinus officinalis*), tanaman aromatik yang banyak digunakan dalam pengobatan tradisional dan formulasi kosmetik, mengandung berbagai senyawa bioaktif dengan potensi manfaat dermatologis. Fitokimia utama yang diidentifikasi dalam rosemary meliputi asam fenolat seperti asam rosmarinat, diterpen seperti asam karnosat dan karnosol, serta flavonoid dan terpenoid volatil. Senyawa-senyawa ini telah menunjukkan aktivitas antioksidan yang kuat dan kemampuan untuk memodulasi jalur molekuler yang terkait dengan penuaan kulit. Bukti dari studi *in vitro* menunjukkan bahwa fitokimia rosemary dapat mengurangi produksi *reactive oxygen species* (ROS), menekan jalur pensinyalan inflamasi, serta menghambat ekspresi MMP yang berperan dalam degradasi kolagen. Studi klinis khususnya dari studi suplementasi oral, juga menunjukkan adanya perbaikan elastisitas kulit, kedalaman kerutan, serta biomarker stres oksidatif, yang mendukung potensi translasi fitokimia rosemary pada kulit manusia. Meskipun studi klinis masih terbatas, bukti yang ada mendukung potensi penggunaan senyawa turunan rosemari dalam formulasi dermatologis dan kosmeseutikal untuk mencegah degradasi kolagen dan pembentukan kerutan. Tinjauan pustaka ini bertujuan untuk menelaah studi terkini mengenai komposisi fitokimia rosemari serta mekanisme molekuler yang mendasari peran senyawa bioaktifnya dalam pencegahan penuaan kulit.

Kata Kunci: Penuaan, Antioksidan, Kolagen, Rosmarinus officialis.

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Introduction

Skin aging is a complex biological process characterized by progressive structural and functional changes in the skin [1]. These changes occur as a result of both intrinsic aging, which is genetically determined and time-dependent, and extrinsic aging caused by environmental factors such as ultraviolet (UV) radiation, pollution, and lifestyle influences [2]. Among the most visible manifestations of skin aging is the formation of wrinkles, which primarily results from the degradation and disorganization of collagen fibers within the dermal extracellular matrix (ECM). As the dermis provides the structural support responsible for skin firmness and elasticity, alterations in dermal collagen integrity is a major contributor of wrinkle development [3].

Collagen is the most abundant structural protein in the dermal ECM, with type I collagen accounting for approximately 80–90% of the dermal collagen content, followed by type III collagen.[4] These fibrillar collagens form a highly organized network that maintains skin tensile strength and resilience. Dermal fibroblasts are responsible for the synthesis and maintenance of this collagen matrix [5]. However, during the aging process, both the production and organization of collagen decline while degradation processes become more prominent [6]. The imbalance between collagen synthesis and degradation leads to thinning of the dermis, fragmentation of collagen fibers, and the formation of wrinkles.[3].

One of the major mechanisms contributing to collagen degradation in aging skin involves the activity of matrix metalloproteinases (MMPs), a family of zinc-dependent endopeptidases that degrade various components of the ECM.[7] Among these enzymes, matrix metalloproteinase-1 (MMP-1), also known as interstitial collagenase, plays a critical role in initiating the cleavage of native type I and type III collagen fibers.[8] Additional MMPs, such as MMP-3 and MMP-9, further contribute to ECM degradation by breaking down collagen fragments and other matrix components.[9]. The expression of MMPs is tightly regulated under normal physiological conditions but can be significantly upregulated in response to oxidative stress, ultraviolet radiation, and inflammatory signalling pathways.[10].

Oxidative stress represents another key contributor to dermal aging and collagen degradation. Reactive oxygen species (ROS), generated through endogenous metabolic processes and environmental exposures such as UV radiation, can disrupt cellular homeostasis and damage macromolecules including lipids, proteins, and DNA.[11] These transcription factors promote the expression of MMPs while simultaneously suppressing collagen synthesis, thereby accelerating the breakdown of dermal collagen and contributing to wrinkle formation. Chronic low-grade inflammation associated with aging further exacerbates this process by promoting the release of pro-inflammatory cytokines that enhance MMP activity [12].

Given the central role of oxidative stress and inflammation in collagen degradation, there has been growing interest in the use of natural compounds with antioxidant and anti-inflammatory properties for the prevention of skin aging. Plant-derived phytochemicals have attracted particular attention due to their diverse bioactive properties and potential for use in dermatological and cosmeceutical applications.[13,14] Many plant polyphenols have been shown to protect dermal fibroblasts from oxidative damage, inhibit MMP expression, and promote collagen preservation [15,16].

Rosemary (*Rosmarinus officinalis*), a perennial aromatic herb belonging to the Lamiaceae family, has long been used in traditional medicine for its antioxidant, antimicrobial, and anti-inflammatory properties.[17] The plant contains a wide range of bioactive phytochemicals, including phenolic acids, flavonoids, and diterpenes.[18] Among the most studied compounds are rosmarinic acid, carnosic acid, and carnosol, which have demonstrated strong antioxidant and cytoprotective activities.[19,20] These compounds have been

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reported to scavenge reactive oxygen species, modulate inflammatory signalling pathways, and potentially regulate the expression of enzymes involved in extracellular matrix degradation.[20,21]

Emerging evidence suggests that rosemary phytochemicals may exert protective effects against skin aging by reducing oxidative stress, inhibiting matrix metalloproteinase activity, and preserving dermal collagen integrity [22,23]. Such mechanisms indicate that rosemary-derived compounds may have promising applications in preventing collagen degradation and wrinkle formation. Therefore, a comprehensive understanding of the molecular mechanisms underlying these effects is essential for evaluating their potential in dermatological and cosmeceutical interventions. This literature review aims to summarize current evidence regarding the phytochemical constituents of *Rosmarinus officinalis* and their potential role in preventing collagen degradation and wrinkle formation through antioxidant, anti-inflammatory, and matrix metalloproteinase-modulating mechanisms.

Methods

This literature review was conducted using a narrative approach to summarize current evidence on the role of Rosmarinus officinalis phytochemicals in preventing collagen degradation and wrinkle formation. A comprehensive search of electronic databases, including PubMed, Scopus, Web of Science, and Google Scholar, was performed to identify relevant studies published up to 2025.

The search strategy employed combinations of keywords and Boolean operators, including: "Rosmarinus officinalis" OR "rosemary," "rosmarinic acid," "carnosic acid," "carnosol," AND "skin aging," "collagen degradation," "matrix metalloproteinase," "MMP," "wrinkle formation," "photoaging," "fibroblast," "oxidative stress," and "antioxidant." Additional articles were identified through manual screening of reference lists from relevant reviews and primary research papers.

The selected studies were analyzed and synthesized qualitatively, with emphasis placed on mechanistic findings and relevance to collagen degradation and wrinkle formation. Systematic review on available clinical trial studies were performed. Datas including study design, population, active compounds, and anti-aging outcome were extracted and presented on a table. No formal meta-analysis was performed due to heterogeneity in study design, models, and outcome measures.

Results and Discussion

Mechanisms of Collagen Degradation in Skin Aging

Collagen degradation is a hallmark of skin aging and plays a central role in the formation of wrinkles and loss of skin elasticity.[24] The structural integrity of the dermis largely depends on the maintenance of ECM components, particularly fibrillar collagen. During the aging process, the balance between collagen synthesis and degradation becomes disrupted, resulting in the progressive breakdown and disorganization of dermal collagen fibers. This imbalance is primarily driven by increased matrix metalloproteinase activity, oxidative stress, and chronic inflammatory signalling, all of which contribute to structural alterations within the dermal ECM.

The dermis is composed predominantly of collagen fibers, with type I collagen accounting for approximately 80–90% of the total collagen content and type III collagen forming a smaller but important fraction that contributes to dermal elasticity and structural flexibility.[5] These collagen fibers are produced and maintained by dermal fibroblasts and form a dense, highly organized network that provides mechanical strength and support to the skin [25]. In youthful skin, collagen fibers are arranged in a tightly packed and well-aligned structure. However, aging leads to fragmentation, thinning, and disorganization of these fibers, which ultimately weakens the dermal matrix [26].

A major mechanism responsible for collagen degradation involves the activity of MMP, a family of zinc-dependent proteolytic enzymes capable of degrading various ECM components. Among them, matrix metalloproteinase-1 (MMP-1), also known as interstitial collagenase, is particularly important because it initiates the cleavage of native fibrillar collagens, including type I and type III collagen.[27] Once the collagen triple helix is cleaved by MMP-1, the resulting fragments become susceptible to further degradation by other MMPs such as MMP-3 (stromelysin-1) and MMP-9 (gelatinase B). The coordinated activity of these enzymes results in extensive breakdown of collagen fibers within the dermal matrix. Under physiological conditions, MMP activity is tightly regulated by tissue inhibitors of metalloproteinases (TIMPs), which maintain ECM

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homeostasis.[28] However, during skin aging, the balance between MMPs and TIMPs shifts toward increased proteolytic activity, favoring collagen degradation. MMP-1 increases in relation to aging [29].

Oxidative stress is another critical contributor to dermal collagen breakdown. ROS, including superoxide anions, hydrogen peroxide, and hydroxyl radicals, are generated through both endogenous cellular metabolism and external environmental exposures [30]. Ultraviolet radiation is considered one of the most significant sources of ROS in the skin and is a major factor in extrinsic skin aging, also known as photoaging.[31] Excessive ROS accumulation can damage cellular components and disrupt normal cellular signalling pathways in dermal fibroblasts. In addition to causing direct oxidative damage to proteins and lipids, ROS can also stimulate the expression of genes involved in ECM degradation.[32]

The induction of MMP expression by oxidative stress is largely mediated through the activation of intracellular signalling pathways. One of the most important pathways involved is the MAPK signalling cascade, which includes extracellular signal-regulated kinase (ERK), c-Jun N-terminal kinase (JNK), and p38 MAPK.[33] Activation of these kinases leads to the stimulation of transcription factors such as activator protein-1 (AP-1).[34] AP-1 plays a crucial role in the regulation of MMP gene expression, particularly MMP-1. When activated, AP-1 binds to promoter regions of MMP genes and enhances their transcription, thereby increasing collagen degradation.[35] Furthermore, AP-1 signalling can simultaneously suppress the synthesis of type I collagen by inhibiting the transforming growth factor-β (TGF-β)/Smad signalling pathway, which is essential for collagen production.[36] As a result, increased AP-1 activity contributes to both enhanced collagen breakdown and reduced collagen synthesis, accelerating the aging process.

In addition to oxidative stress-mediated pathways, inflammatory signalling also contributes significantly to collagen degradation in aging skin. Chronic low-grade inflammation, often referred to as "inflammaging," is characterized by persistent activation of inflammatory mediators and cytokines. Pro-inflammatory cytokines such as tumor necrosis factor-α (TNF-α) and interleukin-1β (IL-1β) can stimulate MMP expression through activation of transcription factors including nuclear factor-κB (NF-κB) and AP-1.[37] These cytokines are frequently elevated in response to environmental stressors, including UV radiation and oxidative damage. The resulting inflammatory environment promotes ECM degradation and further disrupts dermal homeostasis.

Collectively, the combination of oxidative stress, MMP activation, and inflammatory signalling pathways forms a complex molecular network that drives collagen degradation during skin aging. Increased ROS production activates MAPK signalling and transcription factors such as AP-1 and NF-κB, leading to elevated expression of MMPs and suppression of collagen synthesis. At the same time, an imbalance between MMPs and their inhibitors enhances proteolytic activity within the dermal matrix. These processes ultimately lead to fragmentation and loss of collagen fibers, contributing to the structural deterioration of the dermis and the visible appearance of wrinkles.

Phytochemical Composition of Rosemary

Rosemary has been traditionally used in culinary, medicinal, and cosmetic applications, largely due to its high content of bioactive compounds with antioxidant, anti-inflammatory, and antimicrobial properties.[17] The phytochemical composition of rosemary is complex and includes several classes of secondary metabolites, primarily phenolic acids, diterpenes, flavonoids, and volatile terpenoids, as has been described in a study using ultra-high-performance liquid chromatography.[38] These compounds contribute significantly to the biological activities associated with rosemary, including its potential protective effects against skin aging and collagen degradation.

Among the major phenolic compounds present in rosemary, rosmarinic acid is one of the most abundant [38] and extensively studied. Rosmarinic acid is an ester of caffeic acid and 3,4-dihydroxyphenyllactic acid and is widely distributed among plants of the Lamiaceae family including rosemary and lemon.[39] This compound exhibits strong antioxidant activity due to its ability to donate hydrogen atoms and stabilize free radicals.[40] Rosmarinic acid has also been shown to increase endogenous antioxidant expression including glutathione, superoxide dismutase (SOD), and catalase through Nrf2 regulation.[41] In addition to its radical scavenging properties, rosmarinic acid has been reported to possess anti-inflammatory and photoprotective activities, which may contribute to its role in protecting dermal cells from oxidative stress and ultraviolet-induced damage.[42] Other phenolic acids found in rosemary include caffeic acid, chlorogenic acid, and ferulic acid, which also contribute to the plant's overall antioxidant capacity.[43]

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Another important class of rosemary phytochemicals consists of phenolic diterpenes, particularly carnosic acid and carnosol. These compounds are considered the primary lipophilic antioxidants in rosemary and are largely responsible for the plant's strong antioxidant potential.[20] Carnosic acid, which can constitute a significant proportion of the total phenolic content of rosemary leaves, has demonstrated potent free radical scavenging activity and the ability to protect cellular components from oxidative damage.[44] Carnosol, an oxidation product of carnosic acid, also exhibits significant antioxidant and anti-inflammatory properties.[45] Both compounds have been shown to modulate cellular signalling pathways associated with oxidative stress and inflammation, suggesting their potential role in protecting dermal ECM components from degradation.

In addition to phenolic acids and diterpenes, rosemary contains various flavonoids that further contribute to its biological activity. Common flavonoids identified in rosemary include luteolin, apigenin, and diosmetin, along with their glycoside derivatives.[46] These flavonoids possess well-documented antioxidant properties and have been shown to regulate multiple cellular pathways involved in inflammation, oxidative stress, and cell survival.[47] Through their ability to neutralize reactive oxygen species and modulate signalling pathways, flavonoids may play a supportive role in maintaining dermal homeostasis and protecting against environmental stressors that contribute to skin aging.[48].

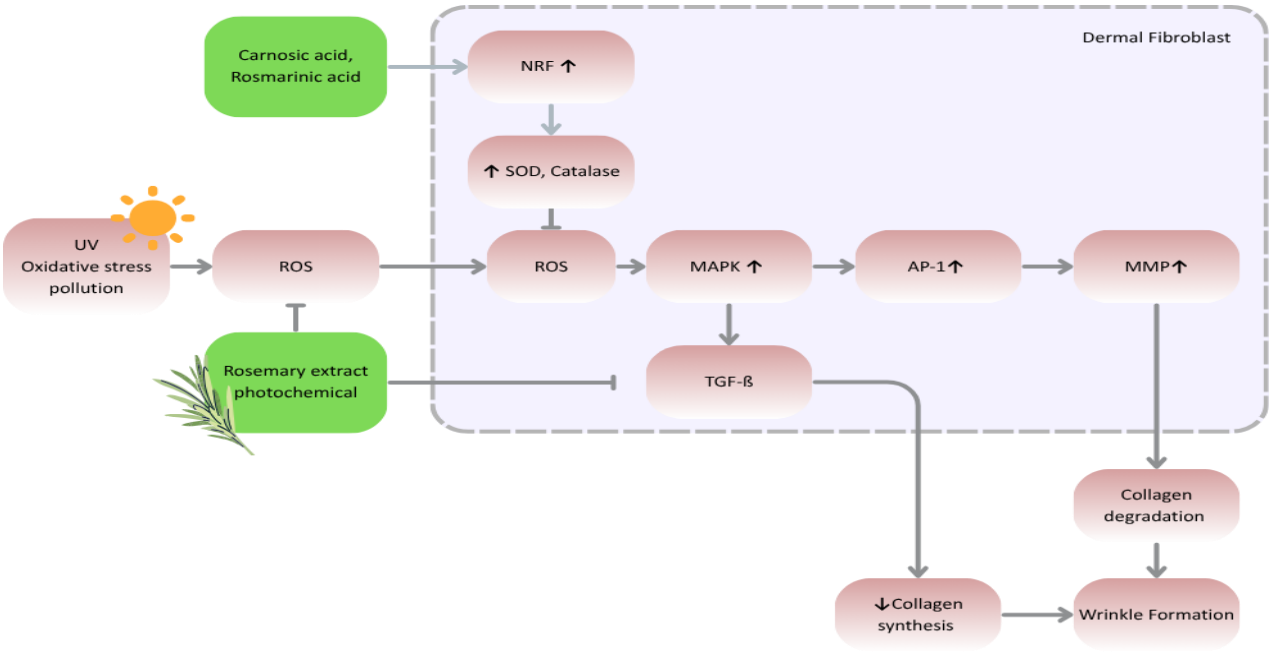

Figure 1. Molecular mechanisms of collagen degradation in skin aging and protective effects of rosemary phytochemicals. Ultraviolet (UV) radiation and environmental stressors induce the production of reactive oxygen species (ROS) in dermal fibroblasts, leading to activation of mitogen-activated protein kinase (MAPK) signaling pathways. This results in activation of transcription factors such as activator protein-1 (AP-1), which upregulates matrix metalloproteinases (MMPs) leading to collagen degradation. Concurrently, oxidative stress and AP-1 signaling inhibit the transforming growth factor-β (TGF-β)/Smad pathway, reducing collagen synthesis. Inflammatory cytokines such as TNF-α and IL-1β further enhance MMP expression via nuclear factor-κB (NF-κB) activation. Collectively, these processes result in extracellular matrix (ECM) degradation and wrinkle formation. Rosemary phytochemicals, including rosmarinic acid, carnosic acid, and carnosol, exert protective effects by scavenging ROS, activating the Nrf2 antioxidant pathway, inhibiting MAPK/AP-1 and NF-κB signaling, and suppressing MMP expression, thereby preserving collagen integrity and mitigating skin aging.

Rosemary also contains a substantial fraction of volatile compounds that constitute its essential oil. These volatile phytochemicals are primarily composed of monoterpenes and other terpenoid derivatives, including 1,8-cineole (eucalyptol), camphor, α-pinene, and borneol.[49] These compounds are responsible for the characteristic aroma of rosemary and exhibit various biological activities, including antimicrobial, anti-inflammatory, and antioxidant effects. Although essential oil components are often more associated with aromatic and antimicrobial properties, some studies suggest that certain monoterpenes may also contribute to photoprotective and anti-inflammatory effects in the skin.[50]

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The phytochemical composition of rosemary can vary considerably depending on several factors, including plant variety, geographic origin, environmental conditions, and extraction methods.[51] Differences in soil composition, climate, harvesting time, and processing techniques can influence the concentration and relative abundance of specific compounds.[52] For example, the levels of carnosic acid and rosmarinic acid may vary significantly between rosemary samples obtained from different regions or extracted using different solvents. Extraction methods such as ethanol extraction, aqueous extraction, or supercritical fluid extraction can also affect the yield and composition of phytochemicals obtained from the plant material. Soxhlet extraction was shown to be the most effective method of extraction to yield the most phytochemical.[38]

Overall, the diverse phytochemical composition of rosemary contributes to its broad spectrum of biological activities. The combined presence of phenolic acids, diterpenes, flavonoids, and volatile terpenoids provides multiple mechanisms through which rosemary may exert protective effects against oxidative stress, inflammation, and extracellular matrix degradation. These properties have led to increasing interest in rosemary as a potential natural ingredient in dermatological and cosmeceutical formulations aimed at preventing collagen degradation and wrinkle formation.

Anti-Aging Mechanisms of Rosemary Phytochemicals

The anti-aging potential of rosemary has attracted increasing scientific interest due to the presence of bioactive phytochemicals that exhibit antioxidant, anti-inflammatory, and cytoprotective activities.[53] Skin aging, particularly wrinkle formation, is largely driven by oxidative stress, chronic inflammation, and degradation of the ECM, especially dermal collagen.[6,11] Rosemary phytochemicals may counteract these processes through multiple molecular mechanisms that collectively contribute to the preservation of dermal structure and function. Among the most prominent bioactive compounds responsible for these effects are rosmarinic acid, carnosic acid, and carnosol, along with several flavonoids and terpenoid constituents.

One of the primary mechanisms through which rosemary phytochemicals exert anti-aging effects is their antioxidant activity. Oxidative stress is a key factor in both intrinsic and extrinsic skin aging, as excessive production of ROS can damage cellular components and activate signalling pathways that promote collagen degradation.[11] Polyphenolic compounds present in rosemary possess multiple hydroxyl groups that allow them to neutralize ROS through electron or hydrogen donation.[43] Rosmarinic acid, in particular, is recognized for its potent radical scavenging activity and ability to reduce oxidative stress in various biological systems. By reducing intracellular ROS levels, rosemary phytochemicals help protect dermal fibroblasts from oxidative damage and maintain cellular homeostasis. Although rosmarinic acid exhibits potent radical scavenging activity in chemical assays, its cellular antioxidant activity may be limited due to poor intracellular accumulation. A study reported that rosmarinic acid was less effective than quercetin in protecting cells from oxidative stress, whereas its metabolite, rosmarinic acid glucuronide, showed comparable activity.[54] This suggests that rosmarinic acid may require metabolic conversion to exert optimal cellular effects. Utilizing rosmarinic acid as therapy require further examination unto its cellular antioxidant property.

In addition to directly scavenging free radicals, rosemary phytochemicals may also enhance endogenous antioxidant defense systems. Rosemary extract was shown to upregulate ARE/Nrf2 in dermal fibroblast, reducing intracellular ROS level, reducing MMP secretion, and improved pro-collagen expression.[55] Certain isolated compounds, particularly carnosic acid and carnosol, have been shown to activate the Nrf2 signalling pathway. Nrf2 is a key transcription factor that regulates the expression of numerous antioxidant and cytoprotective enzymes, including superoxide dismutase, catalase, glutathione peroxidase, and heme oxygenase-1.[56] Activation of the Nrf2 pathway enhances the cellular capacity to neutralize oxidative stress and maintain redox balance.[57] By strengthening endogenous antioxidant defenses, rosemary phytochemicals can reduce oxidative damage to proteins and lipids in the dermal extracellular matrix and limit the oxidative signals that trigger collagen degradation.

Another important mechanism underlying the anti-aging properties of rosemary phytochemicals is the inhibition of MMPs.[58] As discussed previously, MMPs are the primary enzymes responsible for the degradation of collagen fibers in the dermal ECM. Increased expression of MMPs, particularly MMP-1, is strongly associated with photoaging and wrinkle formation.[3] Oxidative stress and ultraviolet radiation stimulate MMP expression through activation of signalling pathways such as MAPK, which subsequently activates transcription factors including AP-1.[59] Several studies have demonstrated that rosemary-derived compounds can suppress these pathways and reduce MMP expression.[22] Rosmarinic acid and carnosic acid have been reported to inhibit MAPK activation, which led to reduced transcription of MMP genes that has been demonstrated in cancer and.[60,61] Inhibition of MAPK pathway is a common mechanism of antioxidant

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mediated therapeutic effect.[62] By limiting MMP-mediated collagen degradation, these phytochemicals may help preserve dermal matrix integrity. In addition to direct inhibition of MMP, this UV mediated increase of MMP-1 may be reduced by increasing Nrf2 expression.[27]

Rosemary phytochemicals also exhibit significant anti-inflammatory properties, which further contribute to their protective effects against skin aging.[63] Chronic low-grade inflammation is increasingly recognized as a major driver of tissue aging, including in the skin. Inflammatory cytokines such as TNF-α and IL-1β can stimulate MMP expression and promote ECM degradation.[37] These cytokines often exert their effects through activation of the nuclear factor-κB (NF-κB) signalling pathway, a central regulator of inflammatory gene expression.[64] Compounds such as carnosol and rosmarinic acid have been shown to inhibit NF-κB activation by preventing the degradation of its inhibitory protein IκB or by suppressing upstream signalling events.[65,66] As a result, the production of pro-inflammatory cytokines and inflammatory mediators is reduced. By attenuating inflammatory signalling, rosemary phytochemicals can help prevent inflammation-induced collagen degradation and maintain dermal structural stability.

Protection against ultraviolet-induced photoaging represents another important aspect of the anti-aging activity of rosemary phytochemicals. Ultraviolet radiation, particularly UVA and UVB, is a major environmental factor responsible for premature skin aging.[67] Exposure to UV radiation leads to the generation of large amounts of ROS in skin cells, which subsequently activate signalling pathways that promote collagen breakdown and inflammatory responses.[68] The antioxidant properties of rosemary compounds enable them to mitigate UV-induced oxidative stress and reduce the downstream activation of MMPs. Some studies have reported that rosemary extracts can protect dermal fibroblasts and keratinocytes from UV-induced damage, partly through suppression of ROS generation and modulation of MAPK signalling pathways.[63] Rosemary diterpenes and flavanone aglycones *in vitro* UV protection has been attributed to its antioxidant capacity.[69,70] A commercially available oral product containing rosemary extract has been shown to reduce UV-induced erythema.[71] This photoprotective effect may contribute to reduced collagen degradation and improved maintenance of dermal ECM structure.

In addition to inhibiting collagen degradation, rosemary phytochemicals may also support the maintenance or enhancement of collagen synthesis. Collagen production in dermal fibroblasts is primarily regulated by the transforming growth factor-β (TGF-β)/Smad signalling pathway, which stimulates the transcription of genes encoding collagen and other ECM components.[72] Oxidative stress and AP-1 activation can interfere with this pathway, leading to reduced collagen production during skin aging. By suppressing oxidative stress and inhibiting AP-1 activity [73], rosemary phytochemicals may indirectly restore or preserve TGF-β signalling and promote collagen synthesis [74], however evidence on skin tissue or cell has not been explored extensively. Although direct stimulation of collagen production by rosemary compounds requires further investigation, the ability of these phytochemicals to reduce inhibitory signals on collagen synthesis suggests a potential role in supporting dermal matrix regeneration.

Furthermore, the synergistic interactions among different phytochemicals present in rosemary may enhance their overall anti-aging effects. The combined presence of hydrophilic polyphenols such as rosmarinic acid and lipophilic diterpenes such as carnosic acid allows rosemary extracts to exert antioxidant activity in both aqueous and lipid environments within the skin.[75] This broad spectrum of activity enables protection of cellular membranes, proteins, and extracellular matrix components from oxidative damage. These hydrophilic and lipophilic property may ease the formulation for topical application. Additionally, flavonoids and terpenoids present in rosemary may contribute complementary biological activities, including modulation of signalling pathways related to inflammation and cellular stress responses that warrants further investigation.[76] Crude extract as a whole, as well as single substance investigation should be carried out simultaneously.

A growing body of experimental research supports the potential anti-aging effects of rosemary and its phytochemicals. Evidence from in vitro experiments, animal studies, and limited clinical investigations suggests that rosemary-derived compounds may contribute to the prevention of collagen degradation and wrinkle formation. In vitro studies using skin-related cell models provide important mechanistic insights into the protective effects of rosemary phytochemicals. Investigations have demonstrated that rosemary extracts and isolated compounds can protect dermal fibroblasts and keratinocytes from oxidative stress and ultraviolet-induced damage.[70,71] Rosmarinic acid has been reported to reduce intracellular ROS levels and improve cell viability in human dermal fibroblasts exposed to oxidative stress.[77] By scavenging ROS and modulating intracellular signalling pathways, rosmarinic acid can attenuate the activation of mitogen-activated protein kinase MAPK signalling and reduce the activity of transcription factors involved in MMP

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expression. Similarly, carnosic acid and carnosol have shown strong antioxidant activity in cellular models and have been reported to activate the Nrf2 pathway, thereby enhancing the expression of endogenous antioxidant enzymes.[78] These effects contribute to reduced oxidative damage and may indirectly limit collagen degradation.

Additional in vitro evidence indicates that rosemary-derived compounds can directly influence the expression of enzymes involved in extracellular matrix remodelling. Studies using UV-irradiated human dermal fibroblasts have shown that rosemary extracts can reduce the expression of MMP-1 and MMP-3 while maintaining collagen synthesis.[71] The suppression of MMP expression appears to be mediated through inhibition of AP-1 and NF-κB signalling pathways, which are known regulators of inflammatory responses and matrix degradation [42], which warrant further investigation. While *in vitro* studies showed promising potential for dermal fibroblas protection against UV, *in vitro* settings may not adequately represent complex tissue environment and the effect of systemic that occurs *in vivo.* Nonetheless, in vitro testing is required to identify the most potent compounds before proceeding to *in vivo* experimentation.

Animal studies have also provided evidence supporting the anti-aging effects of rosemary. In a rat excision diabetic wound model, topical application of Rosmarinus officinalis extract accelerated wound contraction, enhanced re-epithelialization, and increased collagen deposition within the dermal matrix.[79] Similar findings were reported in other rodent studies where rosemary extracts wound healing and, interestingly, prevent fibrosis.[80] These protective effects are largely attributed to the antioxidant activity of rosemary polyphenols, which can reduce reactive oxygen species and suppress inflammatory signaling pathways involved in dermal matrix degradation.[62,77] While the wound healing studies demonstrated increased collagen deposition in diabetic rats, it is important to note that wound healing models represent acute repair processes rather than chronic age-related collagen degradation.[81] The mechanisms and signaling pathways involved in wound healing including inflammatory phase, proliferation, and remodeling)differ substantially from those in chronologically aged or photoaged skin. Therefore, results from wound healing studies should be interpreted cautiously and not be directly extrapolated to anti-aging effects without further validation in appropriate photoaging or natural aging models.

Despite the promising biological activities of rosemary phytochemicals, their successful translation into dermatological and cosmeceutical applications is strongly influenced by formulation-related challenges, particularly skin penetration and compound stability. However studies that assess the stability of topical formulation remains limited. The physicochemical properties of key compounds determine their ability to cross the stratum corneum, which is a highly lipophilic barrier. Rosmarinic acid, a major phenolic constituent, is relatively hydrophilic (low log P, ~0.2–1.0) and has a molecular weight of approximately 360 Da [82], which may limit its passive diffusion through the lipid-rich stratum corneum despite being within the general molecular weight threshold (<500 Da) for skin permeation.[83,84] In contrast, carnosic acid is more lipophilic (log P ~4–5), which may favor membrane partitioning [85]; however, its relatively high lipophilicity can also result in retention within the stratum corneum rather than deeper dermal penetration.[86] Moreover, carnosic acid is chemically unstable and prone to oxidation, leading to degradation into compounds such as carnosol.

To overcome these limitations, advanced formulation should be utilized to enhance dermal delivery. These include lipid-based carriers such as liposomes, ethosomes, and nanoemulsions, which can improve both solubility and skin penetration of hydrophilic and lipophilic compounds.[87] Transdermal penetration of rosmarinic acid ethosome were found to be higher compared to rosmarinic acid liposom on mouse abdominal skin.[88] Despite the possibility of using advanced formulation for rosmarinic and carnosic acid, clinical studies of their efficacy remains limited.

Clinical Evidence

The clinical evidence for rosemary phytochemicals in preventing collagen degradation and wrinkle formation are metodologically varied, as summarised in Table 1. The strongest clinical evidence emerges from oral supplementation studies, which provide compelling support for rosemary's systemic anti-aging effects. A double-blind RCT involving 90 participants demonstrated that oral rosemary-grapefruit polyphenol combinations (Nutroxsun) produced significant wrinkle depth reductions of 8.8–14.8% and elasticity increases of 1.8–4.6% compared to placebo ($p<0.001$), with effects detectable as early as two weeks [89]. Similarly, a placebo-controlled trial of 104 women aged 40-65 years using oral rosemary extract (BioR) showed significant improvements in skin dullness ($p=0.04$), roughness/texture ($p=0.001$), erythema ($p=0.05$), and pore size ($p=0.04$) at 12 weeks [90]. Importantly, this study also demonstrated molecular-level benefits, with significant reductions in oxidative stress markers (4HNE protein adducts) and advanced glycation end products (AGEs)

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in skin biopsies (p<0.005), suggesting that rosemary compounds can reach dermal tissues in therapeutically relevant concentrations when administered systemically.

Table 1. Clinical Evidence of *Rosmarinus officinalis* extract as skin anti-aging agents

Reference	Participant Demographics	Active Compound	Oral or Topical Formulation	Anti-aging Results
Draelos et al, 2025	Age range: 40 to 65 years Gender distribution: Female Baseline skin condition: Moderate-to-severe skin dullness and roughness/texture, mild-to-moderate erythema, pore size, and uneven pigmentation	Rosemary extract (BioR)	Oral capsule; Weeks 1 to 4, two capsules three times daily; Weeks 5 to 8, two capsules twice daily; Weeks 9 to 12, one capsule twice daily.	Significant mean improvements in skin dullness (p=0.04), roughness/texture (p=0.001), erythema (p=0.05), and pore size (p=0.04) at Week 12. Significant mean improvements in global skin quality at Weeks 8 (p<0.0001) and 12 (p=0.002).
Guiotto et al, 2025	Female 40 to 65 years Baseline skin condition: Moderate-to-severe skin dullness and roughness/texture, mild-to-moderate erythema, pore size, and uneven pigmentation	Rosemary extract (BioR)	Oral capsule; Weeks 1 to 4, two capsules three times daily; Weeks 5 to 8, two capsules twice daily; Weeks 9 to 12, one capsule twice daily.	Statistical significance for each anti-aging outcome: Significant reductions in 4HNE protein adducts and AGEs (p<0.005 for biopsies, p<0.05 for tape strips)
Herndon et al, 2015	Female 35-60 years -Baseline skin condition or aging status: Parameters studied included fine lines and wrinkles, clarity/brightness, visual roughness, tactile roughness, evenness of skin tone (redness), evenness of skin tone (hyperpigmentation)	Standardized rosemary leaf extract (ursolic acid) combined with Astragalus membranaceus root extract, a peptide blend, tetrahexyldecyl ascorbate, and ubiquinone	Moisturizer applied twice daily, once in the morning and once in the evening on facial skin for 12 weeks	Statistically significant improvement in all clinical grading parameters at 8 weeks and greater improvement at 12 weeks.
Truchuelo et al, 2025	Healthy female adult aged 25 - 60 years with signs of skin aging (hyperpigmentation, loss of firmness, elasticity, wrinkles)	Combination of polypodium leucotomos extract, glutathione, Rosemary extract, Niacinamide and Magsenium stearate.	Oral capsule, two capsulse per day for 12 weeks	Improved skin hydration of treatment group compared to placebo (p < 0,001), lower pigmentation intensity (p<0,001), improved skin firmness (p <0,001), improvement in wrinkle depth, length, and area (p< 0,001)
Nobile et al, 2016	Female with mean age 52.9, 51.0, and 50.9 years for 100 mg, 250 mg, and placebo groups. Skin phototype I to III (Fitzpatrick classification). Baseline skin condition or aging status: Mild to moderate chrono- or photoageing clinical signs.	Rosemary extract (Rosmarinus officinalis) and citrus extracts (Citrus paradisi)	Oral capsule, 100 mg and 250 mg dose per day	Wrinkle depth decreased by 8.8% to 14.8% in the 100 mg dose group and by 9.1% to 13.9% in the 250 mg dose group over 2 months. Skin elasticity increased by 1.8% to 4.6% in the 100 mg dose group and by 1.5% to 3.7% in the 250 mg dose group over 2 months (p < 0,001). Effects noted as early as 2 weeks after product consumption.

The table presents study characteristics including participant demographics, active compounds, route of administration (oral or topical), and reported anti-aging outcomes. Across studies, rosemary-containing formulations, either as a single extract or in combination with other bioactive ingredients, demonstrated improvements in clinical skin parameters such as wrinkle depth, skin elasticity, hydration, pigmentation, and overall skin quality, as well as reductions in molecular markers of oxidative stress. Abbreviations: 4HNE, 4-hydroxynonenal; AGEs, advanced glycation end products; BioR, proprietary rosemary extract formulation; p, p-value indicating statistical significance.

Limited human topical studies, while methodologically constrained, provide supportive evidence. An open-label trial of 37 women using a multi-ingredient moisturizer containing standardized rosemary leaf extract reported statistically significant improvements in fine lines, wrinkles, roughness, and skin tone at 8 and 12 weeks, though the multi-ingredient formulation prevents attribution of effects specifically to rosemary.[91]

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Aside from anti-aging property, rosemary extract lotion has also demonstrated efficacy toward seborrheic dermatitis, comparable to 2% ketoconazole.[92] Rosemary oil in topical product has also been shown to reduce acne lesions [93] and had activity against *Propionibacterium acnes*.[94] Aside from its antifungal property which has been described [95], efficacy toward seborrheic dermatitis and acne may also be attributed to its anti-inflammatory effect. Rosemary oil has also been studied as hair growth treatment, with a clinical trial demonstrate its efficacy is comparable to minoxidil.[96] Orally administered carnosic acid and rosmarinic acid has been shown to reduce IL-6 expression and collagen degradation following exposure to UVB.[63] These effects are consistent with the known ability of rosemary phytochemicals to modulate inflammatory pathways, including NF-κB signaling.

Safety profiles across all administration routes appear favorable, with topical formulations showing no skin irritation (primary irritancy index <2) and oral supplements demonstrating minimal adverse events, with only one discontinuation due to gastrointestinal upset across 104 subjects. However, the absence of controlled topical RCTs represents a critical limitation in establishing clinical efficacy for direct dermal application, despite the convergent evidence suggesting therapeutic potential for collagen preservation and wrinkle prevention.

Overall, while clinical findings align with mechanistic evidence demonstrating antioxidant, anti-inflammatory, and anti-MMP effects of rosemary compounds, direct clinical validation of their role in collagen preservation and wrinkle prevention remains insufficient. The lack of well-designed randomized controlled trials, particularly for topical formulations, highlights a critical gap between experimental evidence and clinical application. Future studies integrating molecular biomarkers with clinical outcomes are needed to establish a clearer link between the mechanistic actions of rosemary phytochemicals and their therapeutic efficacy in human skin aging.

Conclusions and Future Directions

Overall, rosemary phytochemicals exert anti-aging effects through multiple interconnected mechanisms that target key processes involved in skin aging. Their ability to neutralize reactive oxygen species, activate endogenous antioxidant defenses, inhibit matrix metalloproteinase expression, suppress inflammatory signalling pathways, and potentially support collagen synthesis collectively contributes to the preservation of dermal collagen and extracellular matrix integrity. These multifaceted mechanisms highlight the potential of rosemary-derived compounds as promising natural agents for the prevention of collagen degradation and wrinkle formation, supporting their growing application in dermatological and cosmeceutical formulations aimed at mitigating skin aging.

Emerging clinical evidence further supports these mechanistic findings, particularly from oral supplementation studies demonstrating improvements in skin elasticity, wrinkle depth, and oxidative stress biomarkers. Such findings suggest that rosemary phytochemicals can exert biologically relevant effects in human skin, potentially through systemic antioxidant and anti-inflammatory mechanisms. However, clinical evidence for topical applications remains limited, and the direct translation of these benefits to dermal collagen preservation and wrinkle reduction requires further validation. Therefore, while current data are promising, well-designed clinical trials incorporating both clinical endpoints and molecular biomarkers are needed to substantiate the efficacy of rosemary phytochemicals and bridge the gap between experimental mechanisms and clinical outcomes.

Conflict of Interest

The authors shall declare that there is no conflict of interest.

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