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The Mechanism of Action and Application Prospects of Cornus officinalis and its Active Components in Anti-Photoaging of the Skin

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Abstract
Skin photoaging is primarily caused by oxidative stress, inflammatory responses, and degradation of the extracellular matrix induced by ultraviolet (UV) radiation, making it the main exogenous factor contributing to skin aging. *C. officinalis* is a natural plant whose active components, including flavonoids and polysaccharides, exhibit significant antioxidant, anti-inflammatory, and signal pathway regulatory effects. This review summarises the mechanisms of action of *C. officinalis* and its active components in anti-photoaging, focusing on their ability to delay photoaging by inhibiting photoaging pathways, reducing collagen degradation, scavenging reactive oxygen species (ROS), and regulating the expression of inflammatory factors. It also explores their application prospects in functional skincare products. Existing research indicates that *C. officinalis* and its active components can effectively mitigate the damage caused by photoaging, providing a theoretical basis for the development of natural anti-photoaging formulations.
Keywords: *C. Officinalis*, Photoaging, Mechanism of Action

Introduction

Photoaging is triggered by prolonged exposure to ultraviolet radiation and other external environmental factors. Clinical characteristic changes include deep wrinkles, reduced elasticity, and spotted pigmentation (Wu, S, L., et al. 2002). Skin covers the body surface and serves as the most important window for human interaction with the external environment. During aging, it is highly susceptible to visible changes, directly leading to psychological and social issues such as anxiety, depression, and low self-esteem, which significantly impact people's lives and work. As the global ageing problem becomes increasingly severe, how to delay the onset of ageing, especially how to 'beautify the complexion' and 'preserve skin colour,' has become a focal point of global attention. Therefore, preventing and delaying skin ageing has become one of the hot topics in contemporary medical research (Knezevic et al. 2007).

The core mechanisms underlying skin photoaging involve UV-induced oxidative stress, inflammatory cascades, and extracellular matrix (ECM) degradation. These processes are dependent on the abnormal activation of multiple signaling pathways. The signaling pathways currently known to be involved in skin photoaging include the mitogen-activated protein kinase (MAPK), nuclear factor kappa-B (NF-*κ*B), and Transforming growth factor-β 1 (TGF-β1)/Smad pathways.

Exposure of the skin to UV radiation induces cells to produce ROS, thereby disrupting the body's antioxidant balance. These ROS then stimulate the MAPK pathway and activate the activator protein-1 (AP-1) complex, which is composed of c-Fos and c-Jun. This induces the synthesis of matrix metalloproteinases (MMPs) (Chen et al. 2016). Studies have shown that MMPs can degrade collagen and elastin in the ECM; collagenase MMP-1 is the only MMP capable of degrading intact fibrillar collagen. Other types of MMP, such as gelatinases MMP-2 and MMP-9, can further degrade collagen fragments (Gu et al., 2020). Additionally, NF-κB and AP-1 can reduce the transcriptional levels of TIMPs (Kanta, 2015), and the subsequent decrease in tissue inhibitor of matrix metalloproteinases (TIMPs)/MMPs facilitates further degradation of collagen and elastin.

Concurrently, UV radiation activates keratinocytes and fibroblasts to release pro-inflammatory factors, such as interleukin-1α (IL-1α), Interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α), which recruit inflammatory cells and further amplify the inflammatory response. These inflammatory factors promote the expression of MMPs through pathways such as the activation of NF-*κ*B, thereby accelerating ECM degradation (Wang et al. 2001; Wakisaka et al. 2002).

Previous reviews of anti-ageing plant extracts have usually categorised them according to the chemical composition of their active ingredients, including polyphenols, flavonoids, vitamins, carotenoids, and hydroxy acids. However, few anti-ageing inhibitors have been designed and developed based on the known signaling cascades of skin photoaging. Therefore, researching natural plants that delay skin ageing by regulating these signaling pathways could inform the targeted development of plant extracts for use in anti-ageing cosmetics.

C. officinalis, a natural plant, is the dried flesh of the fruit of the *C. officinalis* plant. To date, 166 major chemical components have been identified in *C. officinalis* herbal medicine, including primarily cycloartenolides (84 types), tannins (29), flavonoids (30), polysaccharides (14), and triterpenoids (9), as well as other components such as alkaloids and monoterpenoids

(Wang et al., 2025). (Wang et al. 2025). These active components exhibit various pharmacological activities, including antioxidant, neuroprotective, cardiovascular protective, hepatoprotective, nephroprotective, immunomodulatory, antitumour, regulation of glucose and lipid metabolism, anti-osteoporotic, anti-inflammatory, antibacterial, antidepressant, improvement of dry eye syndrome, inhibition of melanin, sedative and hypnotic effects, and treatment of hair loss (Chen, et al. 2025). Polysaccharide Co-4, for example, has significant immune-enhancing and anti-aging functions (Hishinuma, K., 2014), while ursolic acid and strychnine have immune-enhancing effects (Ying et al., 2004). The flavonoids in *C. officinalis* primarily inhibit tyrosinase activity to suppress melanin production, thereby providing skin-lightening and whitening effects (Zhang et al. 2009). The total glycosides of *C. officinalis* exhibit anti-inflammatory effects.

The mechanism of action of *C. officinalis* and its active components in regulating photoaging signal transduction pathways

The active components of *C. officinalis* (such as flavonoids, polysaccharides, and cycloartenolides) exert their anti-photoaging effects by targeting the aforementioned pathways, as detailed below.

Inhibiting Oxidative Stress and Scavenging ROS

C. officinalis polysaccharides scavenge hydroxyl radicals and superoxide anions, enhance antioxidant enzyme activity, reduce ROS and malondialdehyde (MDA) levels, and alleviate oxidative stress damage. Li et al. (2015) investigated the effects of *C. officinalis* polysaccharides on oxidative stress responses in the brains of rats with vascular dementia. The results showed that *C. officinalis* polysaccharides activate glutathione peroxidase (GSH-Px) and catalase (CAT), thereby clearing peroxides and alleviating oxidative stress-induced damage.

Studies have shown that applying rutin and naringin to the backs of hairless mice exposed to UVB radiation can reduce UVB-induced ROS and lipid peroxidation (Martinez et al. 2016). Cell experiments with naringin, quercetin, and cyanidin-3-O-glucoside (C3G) indicate that flavonoids can reduce intracellular ROS levels and thereby reduce deoxyribonucleic acid (DNA) damage. They can also prevent ROS attacks on cell membranes and mitochondria, inhibit the release of cytochrome c and thus inhibit apoptosis (Zhu et al., 2017 and Hu, et al. 2016).

Li et al. (2012) investigated the in vitro antioxidant activity of the polysaccharides PFCA-III and PFCC-I from *C. officinalis* and found that both effectively scavenge hydroxyl radicals and superoxide anions.

Inhibiting inflammatory Responses and Downregulating Pro-Inflammatory Factors

Xu, et al. (2025) investigated the effects of *C. officinalis* extract on UVB-induced human keratinocytes (HaCaT) and mice. The study found that *C. officinalis* extract significantly reduced the messenger ribonucleic acid (mRNA) and protein levels of MMP-1, MMP-3, and MMP-9 in UVB-induced HaCaT cells, while increasing the expression of type I and type III collagen.

Quercetin competitively binds to adenosine triphosphate (ATP), weakens $p90^{RSK}$ phosphorylation, downregulates AP-1 activity, and inhibits MMP-1 expression. When quercetin was applied to the backs of SKH-1 hairless mice, it was found to significantly inhibit UVB-induced extracellular regulated protein kinases 2 (ERK2) activity, weaken UVB-induced $p90^{RSK}$ phosphorylation by competitively binding to ATP, reduce the stability of the immediate early gene Fos-related antigen-1, downregulate AP-1 activity, and subsequently reduce MMP-1 expression, thereby exerting an effective anti-photoaging effect (Jung et al. 2016).

Intervention in Key Signaling Pathways for Anti-Aging MAPK Signaling Pathway, NF-κB Signaling Pathway, TGF-β1/Smad Signaling Pathway

MAPK signaling pathway: *C. officinalis* flavonoids can reduce MMP transcription by inhibiting the MAPK/AP-1 pathway. Studies have shown that oral administration of naringin to hairless mice reduces UVB-induced MMP-9 expression by inhibiting the phosphorylation of methyl ethyl ketone (MEK)/ERK in the MAPK signaling pathway, thereby achieving a preventive effect against photoaging (Lee, et al. 2018).

NF-*κ*B pathway: By applying non-steroidal anti-inflammatory drugs to the backs of SKH-1 hairless mice, it was found that they can inhibit the levels of inflammatory cytokines TNF-α, IL-1β, and IL-6 by inhibiting the intracellular phosphatidylinositol 3-kinase (PI3K)/protein kinase B (Akt)/NF-*κ*B pathway, reduce cyclooxygenase-2 (COX-2) expression, thereby lowering prostaglandin E2 (PGE2), and ultimately suppress UVB-induced inflammation (Pal, H. C., et al. 2015).

TGF-β1/Smad pathway: The flavonoid compound HMF (3,5,6,7,8,33,4'-heptamethoxyflavone) can regulate the TGF-β/Smad signaling pathway, inhibiting Smad7 expression, upregulating Smad3 expression, thereby upregulating the transcription of TGF-β-regulated genes, and increasing the expression of type I procollagen-related genes, indicating that flavonoids have anti-photoaging effects on the skin (Kim, H. I., et al. 2018). Kang, Y., et al. (2015) also found that appropriate concentrations of GSP significantly upregulate the level of transforming growth factor-β receptor II (TGF-BRII) protein in human dermal fibroblast (HDF) cells and downregulate the expression of Smad7, thereby alleviating UVA-induced degradation of the extracellular matrix.

Conclusions & Suggestions

In summary, this review summarises the mechanisms of action and application prospects of *C. officinalis* and its active components in anti-photoaging of the skin. Photoaging of the skin is triggered by prolonged ultraviolet radiation, with the core mechanisms involving abnormal activation of the MAPK, NF-*κ*B, and TGF-β1/Smad signaling pathways, leading to oxidative stress, inflammatory responses, and degradation of the extracellular matrix. *C. officinalis* contains 166 major chemical components, including flavonoids and polysaccharides, which exert their effects through multiple mechanisms. At the molecular level, polysaccharides scavenge free radicals and activate antioxidant enzymes, while flavonoids reduce ROS production to inhibit oxidative stress. In terms of inflammation regulation, the extract reduces MMP expression and increases collagen content, while quercetin downregulates inflammatory damage by inhibiting related activities. In signal pathway intervention, it can target the MAPK pathway to inhibit MMP transcription, target the NF-*κ*B pathway to reduce inflammatory factor levels, and target the TGF-β1/Smad pathway to promote collagen synthesis. These synergistic effects of multiple components and multiple targets provide a systematic theoretical foundation and experimental basis for the development of natural anti-photoaging formulations.

Building on this foundation, we will utilise the three key advantages of *C. officinalis* to develop anti-photoaging skincare products: its well-defined, multi-target mechanism; its high safety profile; and its strong synergistic effects with traditional ingredients. Moving forward, our focus will be on researching and developing natural anti-aging skincare products using new processes and technologies. For example:
we will combine the multiple active components of *C. officinalis*:

- through a targeted transdermal delivery system to develop a *C. officinalis* hydrogel sustained-release mask.
- with other ingredients that have anti-ageing and moisturising effects to develop a multi-pathway synergistic anti-aging serum.
- to develop natural sunscreens containing the photoprotective active components of *C. officinalis*.

In summary, enhancing the bioavailability of product ingredients, optimising their stability, and improving their anti-photoaging efficacy are key technical considerations in developing *C. officinalis*-based anti-photoaging skincare products. There is significant future market demand for new, natural, and side-effect-free skincare products made from natural ingredients.

Against the backdrop of accelerating global ageing, unprecedented consumer focus on skin health and appearance, and surging demand for ‘clean beauty’ and natural ingredient skincare products, this study systematically integrates the multi-targeted, multi-level mechanisms of action of *C. officinalis* and its various active components in combating skin photoaging. It explores its application prospects, making significant theoretical and contextual contributions.

Deepens understanding of the mechanisms of natural plant-based anti-photoaging: This study innovatively focuses on a single traditional medicinal plant, *C. officinalis*, to deeply explore the specific molecular mechanisms by which its multiple active components synergistically act on the core signaling pathways of skin photoaging. It constructs a relatively complete ‘component-target-pathway-effect’ action network model, significantly enriching the theoretical foundation of natural products for anti-skin aging.

Providing a model for the development of ‘multi-component-multi-target’ natural plant-based cosmetics: *C. officinalis* itself contains multiple active substances with potential anti-photoaging properties. The study not only outlined the individual functions of these components but also emphasised their potential to synergistically act on key stages of photoaging through different mechanisms. This provides important theoretical basis and design concepts for developing photoprotective formulations based on natural plant composite systems with synergistic multi-functional effects, aligning with current trends in natural product research and development.

It points the way toward developing efficient and safe natural anti-photoaging strategies: This study thoroughly demonstrated the efficacy of *C. officinalis*'s active components in anti-photoaging and their relative safety advantages as natural plant-derived compounds. Additionally, by closely integrating modern formulation technology and market demands, it provides a clear technical pathway and market positioning for advancing *C. officinalis* from laboratory research to actual product development, thereby meeting consumer demand for efficient, natural, and gentle anti-aging products.

In summary, this study not only deepens our scientific understanding of the anti-photoaging mechanisms of *C. officinalis* but also holds significant theoretical and practical implications, bridging traditional Chinese medicine wisdom with modern dermatology. It addresses the market demand for natural, efficient anti-aging products and drives the development of related industries.

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