

Review

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Review

## Exploring Artemisia for Skin Diseases: A Natural Approach to Dermatological Therapy

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Abstract: Skin conditions, varying from minor irritations to serious inflammatory and infectious disorders, significantly impact human health and quality of life. Traditional herbal medicine has always been a source of therapeutic agents for the treatment of skin diseases, and the genus *Artemisia* has become a valuable resource due to its rich diversity of bioactive compounds. This review details the historical context and antibacterial activities of various *Artemisia* species used in dermatological therapy. Various species have been found to be effective against specific dermatological conditions, including *A. argyi* and *A. princeps* against contact dermatitis, *A. annua*, *A. capillaris*, *A. anomala* and *A. apiacea* against atopic dermatitis and *A. lavandulaefolia* against rosacea. In addition, *A. annua* has therapeutic efficacy against eczema, *A. dracunculus* L. against leishmaniasis and skin cancer, and *A. arborescens* against psoriasis treatment. *A. annua* and *A. capillaris* are included in broader dermatological applications including UV-induced skin diseases where *A. scoparia*, *A. iwayomogi*, and *A. asiatica* have been shown to have promising activity. The cosmetic benefits of *Artemisia* species such as *A. iwayomogi* for anti-aging and *A. argyi* for moisturizing also make them sought after in skin care products. Moreover, this review considers the tyrosinase activity of *Artemisia* species germinated in Kazakhstan and further defines the dermatological significance of the genus.

Keywords: Artemisia; skin disease; antibacterial; atopic dermatitis; skin cancer; skin inflammation

#### Methods Used in the Review

This study used the scientific databases PubMed, SciFinder, and Google Scholar for a literature search of relevant studies that contained the keywords "skin diseases", "artemisia species", "skin cancer", "artemisinin", "antibacterial", "dermatology", "skin", and "skin disorders". All search terms were used in various combinations, and studies were screened for relevance based on their abstracts. A review of studies written in English and Russian languages were considered. The bibliographical



analysis indicated a total of 26 genera belonging to *Artemisia* family that was used against skin related diseases.

#### Introduction

Skin diseases affect more than 20% of the world's population, exercising a considerable burden on public health [1,2]. The economic implications of skin conditions are significant, particularly with human skin wounds as a growing concern [3]. In addition, the psychological impact of these diseases is deep, influences mortality in mental disorders [4]. The incidence of non -melanoma skin cancer is increasing worldwide [5], while psoriasis remains frequent and widely studied [6]. World Health Organization emphasizes the importance of addressing environmental risks to mitigate health loads [7]. As treatments evolve, the understanding of adverse effects remains critical [8,9].

Eczema, psoriasis and vitiligo are prevailing skin conditions that significantly affect the quality of life of patients. These disorders arise from complex interactions between genetic, environmental and immunological factors, which leads to abnormal skin responses. The pathophysiology of eczema, mainly identified as atopic dermatitis, implies a compromised skin barrier and an abnormal immune response characterized by high levels of IgE and an influx of TH2 cells [10]. Psoriasis, in contrast, is characterized by hyperactivation of the immune system, particularly that involves TH1 and TH17, leading to a greater proliferation of keratinocytes [11]. Vitiligo is considered an autoimmune disorder where there is a loss of melanocytes due to a deregulated immune system that addresses these pigment producing cells (Figure 1) [12].

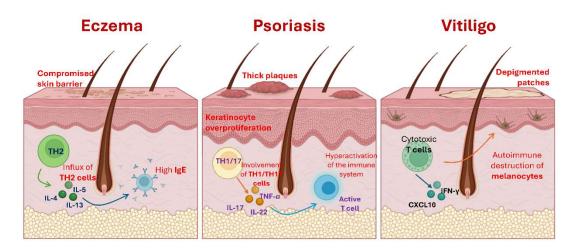


Figure 1. Simplified Immunological Pathways in Skin Disease Progression.

The prevalence of these skin conditions varies significantly between populations. It is reported that the eczema affects approximately 10-20% of children and 1-3% of adults [13]. Psoriasis occurs in approximately 2-3% of the population, with implications for life for many affected individuals [14]. Vitiligo impacts between 0.5-2% of the global population, with variations based on ethnicity and geographical distribution [15]. These statistics underline the generalized nature of these conditions and the need for effective treatment strategies to relieve the anguish they cause.

Eczema treatment options generally involve topical moisturizing and corticosteroid agents to control inflammation and restore the skin barrier [16]. Systemic therapies, including immunosuppressants, are reserved for severe cases. In psoriasis, patients can benefit from topical treatments, phototherapy or systemic medications, including biological ones that go to specific immune paths such as IL-17 and IL-23 [17]. Vitiligo treatments often include topical corticosteroids, phototherapy with narrow band UVB and emerging therapies such as immune modulators [18]. However, responses to treatments can be variable, and not all patients achieve satisfactory results.

In this review are given the types of *Artemisia* that have potential for use treatment in skin diseases and cosmetics. Ethnopharmacological studies reveal that the components of *Artemisia* 

species can effectively modulate skin conditions through various biochemical paths, indicating their role as promising candidates for the development of natural dermatological therapies.

#### Historical Background of Artemisia in the Treatment of Skin Diseases

About 2,500 plants known to have been used in traditional medicine in Russia and Central Asia, about 1,000 have been used to treat various skin diseases. Some plants, however, are much more widely used to treat skin diseases than others, and about 300 medicinal plants are known to have been frequently used in prescription and over-the-counter pharmaceuticals in post-Soviet states. The genus Artemisia (family: Asteraceae) encompasses a diverse group of plants widely distributed across temperate regions of the Northern Hemisphere. Comprising over 500 species, Artemisia is recognized for its extensive medicinal properties, which have been traditionally exploited in various cultures. Russia and China exhibit the highest species diversity. In Kazakhstan, 81 species have been documented, including 19 endemic species, with 34 of these occurring within Central Kazakhstan [19–21]. The genus has a significant historical and cultural value in traditional medicine, in particular for the treatment of skin diseases. The effectiveness of Artemisia species in the management of skin diseases can be attributed to their rich phytochemical composition. Compounds such as flavonoids, terpenoids and essential oils have notable anti-inflammatory, antibacterial, antiseptic and antioxidant properties [22]. These bioactive constituents promote the healing of wounds and reduce the symptoms associated with various dermatological conditions, including eczema and psoriasis. For example, traditional methods often involve the topical application of extracts or plant material finely on the ground in affected areas, which has demonstrated significant health benefits in clinical observations [23]. Current research reaffirms the relevance of Artemisia in therapies based on contemporary plants, in particular as a natural alternative to synthetic pharmaceuticals. In recent years, studies have highlighted not only traditional uses but also the pharmacological properties of Artemisia species, supporting their inclusion in modern treatments for skin evils [24]. In addition, the exploration of Artemisia's potential as a source of cosmetic raw materials highlights its versatility and its meaning in medicinal and beauty applications [25].

**Table 1.** Traditionally used *Artemisia* species in skin disorders.

Species name	Part used	Traditional use	Country	Reference
Artemisia iwayomogi		skin whitening, itchy skin	Korean folk medicine	[26]
Artemisia argyi		itchy skin, eczema	Traditional Chinese, Japanese and Korean medicine	[27]
Artemisia princeps		itchy skin, eczema	Traditional Chinese, Japanese and Korean medicine	[27]
Artemisia herha-alha	essential oil from the leaves and the thin branches	local skin infections	;	[28]
Themom nerva area		skin diseases, scabies	Jordanian traditional medicine	[29]
Artemisia ahsinthium	Herb	boils, wounds, and bruises ulcerative sores,	Poland and Ukraine	[30]
Artemisii uosininium		eczema, purulent scabies		[31]

Artemisia vulgaris		ulcerative sores, eczema, purulent scabies		[31]
Artemisia annua		eczema, scabies, sores	Traditional Chinese medicine	[32]
Artemisia arborescens		Psoriasis	Southern Italy	[33]
Artemisia dracunculus		skin wounds, irritations, allergic rashes, and dermatitis	Asia, Russia	[34]
Artemisia capillaris		skin inflammation	Traditional Chinese medicine	[35]
Artemisia anomala		wound-curing agent	Traditional Chinese medicine	[36]
Artemisia apiacea		eczema and jaundice	Traditional Chinese, Japanese and Korean medicine	[37]
Artemisia asiatica		skin health and increase the elasticity of skin	Traditional Korean medicine	[38]
	Leaves	carbuncle and boil in skin, itchy skin	Traditional Chinese medicine	[38]

#### Antibacterial Potential of Artemisia Species

There has been a surge in interest in medicinal plants that have antimicrobial or antibacterial properties as a means of combating antibiotic-resistant infections, which have become an increasingly serious health threat worldwide. There is an increasing recognition that antibiotic resistance represents a significant public health issue, with genetic mutations and horizontal gene transfer providing mechanisms through which pathogenic microorganisms acquire resistance to conventional antibiotics [39,40]. In this regard, there is growing interest in the study of natural products derived from plants, which are known to contain a diverse range of bioactive compounds with potent antibacterial, antifungal and antiviral properties that may offer a promising alternative or complementary approach to traditional antibiotic therapy [41,42]. These plant-derived compounds featuring the capacity to synthesize enzymes that are capable of tearing apart microbial cell membranes, halting protein production, or inhibiting microbial enzymes is very relevant today. Moreover, the therapeutic effects of these compounds may greatly contribute to reducing the consequences of antibiotic resistance and fighting infections produced by multi-drug resistant bacteria [43,44]. Medicinal plants are rich in secondary metabolites, including alkaloids, flavonoids, terpenoids, phenols, and saponins, which have bacteriostatic effects, inhibiting bacterial growth, or bactericidal effects, directly killing bacteria [45,46]. These compounds act on bacterial cell walls, membranes, or genetic material and modulate virulence factors such as biofilm formation and quorum sensing, which are often linked to resistance mechanisms [47,48]. Bacterial infections represent a prominent etiological factor in dermatological disorders, ranging from mild irritations to severe systemic diseases [49]. Among the most prevalent bacterial pathogens, Streptococcus and Staphylococcus species are of particular significance in the pathogenesis of various cutaneous infections [50]. Cutaneous conditions associated with Streptococcal infections encompass pyoderma, streptoderma, and streptococcal impetigo. Streptococcus pyogenes is an important cause of skin diseases, in particular impetigo, cellulite and necrotizing fasciitis. This bacterium enters the skin by cuts, blisters or insect bites, leading to various infections [51]. The pathogenic mechanisms of S. pyogenes involve the production of toxins and enzymes which can damage skin tissue and escape the immune system [52]. Staphylococcal infections, predominantly attributed to Staphylococcus aureus, are

associated with a variety of skin conditions, such as impetigo, folliculitis, furuncles, and subcutaneous abscesses [53]. Furthermore, the production of exfoliative toxins by *S. aureus* is implicated in the development of staphylococcal scalded skin syndrome [54]. The clinical manifestations of these infections exhibit a broad spectrum of severity, affecting individuals with both intact and compromised immune systems [53]. At present, *S. aureus* infections are treated with antibiotics, and there has been a dramatic rise in antibiotic-resistant strains, including methicillin-resistant *S. aureus* (MRSA) [55]. This growing resistance emphasizes the need for novel therapeutic strategies, improved infection control measures, and judicious use of existing antibiotics to mitigate the spread and impact of these resistant strains [39].

**Table 2.** Antibacterial and antimicrobial activities of *Artemisia* species against *Staphylococcus aureus* and *Streptococcus pyogenes* bacteria.

Species name	Part used	Bacteria	Referenc	
Artemisia scoparia	essential oil	S. aureus	[56]	
Artemisia oliveriana Artemisia aucheri	ethanol extract	S. aureus	[57]	
Artemisia absinthium	in vivo	S. aureus S. pyogenes	[58,70]	
Artemisia afra	ethanol, methanol, and n- hexane extracts of leaves	S. aureus	[59]	
Artemisia vulgaris	aqueous, ethanol, petroleum ether and benzene extract of leaves	S. aureus	[60]	
Artemisia asiatica	essential oil from leaves	S. aureus S. pyogenes	[61]	
Artemisia annua	essential oil	S. aureus	[62,63]	
Artemisia princeps	ethanol extract	S. aureus	[64]	
Artemisia abrotanum	ethanol extract	S. aureus	[65]	
Artemisia lerchiana	infusion and essential oil extract	S. aureus Streptococcus	[66]	
Artemisia nilagirica	essential oil	S. aureus S. epidermidis	[67]	
Artemisia judaica	essential oil	S. aureus	[67]	
Artemisia ifranensis	essential oil	S. aureus	[67]	
Artemisia herba-alba	essential oil	S. aureus	[68]	
Artemisia gmelinii		S. aureus S. epidermidis S. pyogenes	[67]	
Artemisia fragrans	essential oil	S. aureus S. epidermidis	[67]	
Artemisia dracunculus	essential oil	S. aureus	[67]	
Artemisia campestris	essential oil	S. aureus	[69]	
Artemisia argyi	chloroform fraction from aqueous extract	S. aureus	[67]	
Artemisia apiacea	ethanol extract of aerial parts	S. aureus	[67]	

There are numerous conditions that can adversely affect the skin, with over a thousand potential causes. Nevertheless, dermatological diseases may arise from various factors, including parasitic, bacterial, and fungal infections, as well as immune system deficiencies and prolonged exposure to ultraviolet (UV) radiation. Many common skin disorders have effective herbal treatment options available. The following section outlines potential *Artemisia* species.

#### Contact Dermatitis

#### Artemisia argyi and Artemisia princeps

Yun et al. investigated two representatives of *Artemisia* species (*Artemisia argyi* and *Artemisia princeps*) based literature background of plants in traditional medicine and studied biological activities. *Artemisia* leaf extract was tested in vitro and in vivo for its anti-inflammatory activity on Raw 264.7 cells and mice with 1-fluoro-2,4-dinitrobenzene-induced contact dermatitis. Therefore, *Artemisia* leaf extract inhibited the release of NO and PGE2 in response to the inflammation, and also decreased the content of TNF- $\alpha$ , IFN- $\gamma$  and IL-6 in inflamed tissues, which prevented epidermal hyperplasia and immune cell infiltration. The extract was found to be effective when applied to induced mice and can be utilized to treat contact dermatitis people with it [27].

#### Atopic Dermatitis

#### Artemisia annua

Studies have shown the effects of *A. annua* aqueous extract on a mice model of atopic dermatitis caused by 2,4-dinitrochlorobenzene (DNCB). Applying DNCB to the ears of BALB/c mice resulted in the development of notable clinical signs that resembled atopic dermatitis, such as redness, swelling, ulceration, and dry, flaky skin. There was a significant reduction in clinical skin parameters following treatment with *A. annua* aqueous extract. Also, the treatment significantly reduced the size and weight increase of the spleen caused by DNCB-induced inflammatory alterations in mice, particularly when administered at higher dosages. The mechanism of atopic dermatitis processes has been evaluated because of the relationship between immunological and inflammatory manifestations and the condition's progression. A study found that the plant extract suppressed symptoms by inhibiting p38 MAPK and NFkB signal pathways. As a result of these observations, it was clear that *A. annua* aqueous extract could relieve atopic dermatitis symptoms in mice [32].

#### Artemisia capillaris

Artemisia capillaris was assessed for its ability to inhibit inflammatory processes in vitro by assessing of nitric oxide by lipopolysaccharide-stimulated RAW264.7 cells and histamine by PMA/A23187-stimulated MC/9 mast cells. As result, *A. capillaris* extract dramatically decreased LPS-induced nitric oxide and suppressed histamine synthesis in MC/9 cells stimulated by PA. In vivo evaluation of *A. capillaris* extract has been conducted on Nc/Nga mice induced by the house dust mite *Dermatophagoides farinae*. *A. capillaris* extract was applied externally to mice's backs and ears for a period of four weeks, and by the third week of treatment, the severity of dorsal skin and ear lesions had been greatly minimized, indicating a possible therapy for treating symptoms of atopic dermatitis [71].

#### Artemisia anomala

There has been a long history of *Artemisia anomala* use in Chinese, Korean, and Japanese medicine to treat inflammatory diseases. Nevertheless, there is still a lack of knowledge regarding the mechanisms by which *A. anomala* can be therapeutically effective in atopic dermatitis. In accordance with this comprehension Yang et al. examined the anti-inflammatory properties of the ethanol extract from *A. anomala*, especially the effects in a mouse model of DNCB-induced atopic

dermatitis and TNF- $\alpha$ /IFN- $\gamma$ -stimulated HaCaT cells. In contrast to the control group, mice treated with *A. anomala* ethanol extract had significantly improved skin conditions and considerably reduced epidermal thickness of their dorsal skin. According to this, *A. anomala* may have potential as a therapy for atopic dermatitis [36].

#### Artemisia apiacea

Artemisia apiacea ethanol extract was evaluated in vitro and in vivo for its anti-inflammatory properties in HaCaT cells, as well as its potential as an atopic dermatitis treatment in a mouse model induced by DNCB. The results of both analyzes showed that the plant extract regulates the production of cytokines and chemokines through the p38/NF-κB pathway, and also relieves symptoms of skin lesions in mouse models, such as dorsal skin thickness and ear skin thickness. Although more research is needed, this study points to the fact that *A. apiacea* can be used therapeutically in the treatment of atopic dermatitis [37].

#### Rosacea

#### Artemisia lavandulaefolia

There has been recent research investigating *A. lavandulaefolia's* in vitro anti-rosacea properties. It has been demonstrated that two chlorogenic acid isomers isolated from a 40% ethanol extract efficiently suppress the activity of KLK5, which is an essential intermediary of rosacea-related inflammatory and vascular processes. By inhibiting KLK5, LL-37 is converted from inactive cathelicidin into active form, regulating immune function and blood vessel function. In addition, isochlorogenic acids have been studied in terms of their mechanisms of action. Several studies have been conducted on isochlorogenic acids to find out how they act. These findings suggest rosacea may benefit from using the plant as a therapeutic agent [72].

#### Eczema

#### Artemisia annua

There has been a research study looking at the potential therapeutic effects of the aqueous extract of *Artemisia annua* against eczema using a 3D in vitro epidermal inflammation model and an in vivo itching model in animals suffering from eczema of topical preparation containing *A. annua* aqueous extract. As demonstrated in the study, topical preparation containing *A. annua* aqueous extract has a similar antipruritic effect to clinical anti-eczema medication – clobetasol propionate ointment. Consequently, the increase in itch threshold suggests *A. annua* aqueous extracts could be anti-eczema and these findings suggest their potential for treatment [73].

#### Leishmaniasis

#### Artemisia dracunculus L.

An ethanolic extract of *Artemisia dracunculus* L. dissolved in dimethyl sulfoxide was evaluated for its antileishmanial effect in vitro. The experiment was carried out at various parasite concentrations (100–1000  $\mu$ g/ml) for three days, recording the results every 24 hours, and the corresponding IC50 were 962.03, 688.36 and 585.51  $\mu$ g/ml. According to repeated-measures analysis, *A. dracunculus* extract showed a significant difference in the interaction between concentration and time with P < 0.05. Results from this study suggest that *A. dracunculus* extract may be used in conjunction with or as an alternative treatment for cutaneous leishmaniasis [74].

#### Skin Inflammation

#### Artemisia capillaris

This study analyzed the literature regarding *Artemisia capillaris* which is widely recognized in traditional Chinese medicine for its ability to cure skin inflammatory diseases and anti-inflammatory properties of its components. According to in vitro and in vivo studies, the plant and its several main components (esculetin and quercetin) revealed a potential inhibitory effect against 5-lipoxygenase considering that it is a leukotriene-producing enzyme that is closely associated with inflammation of the skin. Based on these results, inflammatory skin problems of the skin can be effectively treated with the help of this plant material [35].

#### Artemisia annua

Artemisia naphtha is a byproduct of artemisinin extraction and an oil consisting of camphor, camphene, p-cymene, eucalyptol, and D-limonene as its main constituents identified by GC-MS. The study demonstrates the anti-inflammatory and antimicrobial activity of the oil extract by suppressing the microbial pathogens that cause acne and eczema. Moreover, human clinical trials indicate that Artemisia naphtha oil is effective in reducing symptoms of acne and eczema when applied locally for 2 weeks at a 1% concentration to acne-prone skin. These in vitro analysis and clinical evidence demonstrate the efficiency in the treatment of problem skin [75].

#### Psoriasis

#### Artemisia arborescens

Bader et al. conducted an experiment on *Artemisia arborescens* along with other plants against psoriasis and other skin diseases caused by an unbalanced eicosanoids production. Since dermatological diseases, including psoriasis, are associated with eicosanoids which contribute to innate immunity. The results indicate that *A.ligustica* extract enhances the biosynthesis of 15(S)-HETE. Researchers have studied the activation of nuclear factor kappaB (NF $\kappa$ B), and it has been shown to have NF $\kappa$ B inhibitory activity [76].

#### UV-Induced Skin Diseases

#### Artemisia scoparia in a Complex

An investigation of *Artemisia scoparia* in conjunction with other herbal plants has been conducted to explore its inhibitory effect on UVB-induced photoaging and the mechanism of action. The complex was prepared from *A. scoparia, Limonium tetragonum, Triglochin maritimum* and red ginseng root by ethanol (50%) extraction. As a result, the complex demonstrated increased survival in HaCaT cells stimulated with 100 mg/ml tert-butyl hydroperoxide (tBHP) which has been found to induce oxidative stress and cell destruction. Moreover, the treatment with the complex resulted in significant increases in collagen synthesis and restoration of collagen and elastin degradation caused by UVB-induced cell damage. The complex inhibits matrix metalloproteinase production by inhibiting MAPK/NFkB signaling at the level of cells [77].

#### Artemisia iwayomogi

In light of the fact that skin is subject to oxidative damage when exposed to UV irradiation, researchers have studied polysaccharides, which are powerful antioxidants. The object of the study is polysaccharides from *Artemisia iwayomogi* stem obtained by ethanol extraction and fractionation with water. According to the study, polysaccharides from *A. iwayomogi* stems showed the highest hydroxyl and superoxide radical scavenging activity with 66.14% and 74.40% at 100 mg per 3 mL concentration. Animal skin tissues were also significantly protected by polysaccharides of *A. iwayomogi* against UVB damage caused by protein oxidation and lipid peroxidation. Moreover, the inhibitory effect on reactive oxygen species (ROS) produced in human neutrophils was investigated with 83.14% at 20 µg per well, indicating high ROS scavenging ability [78].

#### Artemisia asiatica

Pharmacological studies evaluated protective effect of *Artemisia asiatica* ethanol extract on UVB-induced cell death in keratinocytes, as well as cytotoxicity, *moisturizing factors*, expression of matrix metalloproteinases (MMPs) genes and inflammatory genes as COX-2 in HaCaT, B16F10, HEK293 and NIH3T3 cells. It was found that the plant extract was not cytotoxic and protected various types of cells from UV-mediated cell death, restored procollagen type 1 gene expression, and reduced MMPs and COX-2 expression. Additionally, the expression of tyrosinase and melanin secretion induced by  $\alpha$ -MSH at a concentration of 50  $\mu$ g/ml were also significantly suppressed in B16F10 cells. The cumulative result of research using variety of photoaging methods and studying the mechanisms leads to the fact that the *A. asiatica* ethanol extract may become a protective agent for the skin [38].

Skin Cancer

#### Artemisia dracunculus L.

Over 3.000 plant species worldwide have anti-cancer properties, which contribute 60% of anti-cancer agents today. Medicinal plants are considered as beneficial chemicals for the making of novel chemotherapeutic drugs and an example of them can be *Artemisia dracunculus* L., which has antitumor properties [79]. One study conducted an in vivo study of the chemopreventive effects of a methanol extract of *A. dracunculus* on skin cancer caused by 7,12-dimethylbenzeanthracine in 18 adult male Balb/c mice divided into 3 groups. As results, the treatment revealed significant reduction in tumor incidence, tumor volume and tumor burden after oral administration at a dose of 500 mg/kg/d. In fact, the study was carried out on the basis that three flavonoid compounds, namely rutin, quercetin and kaempferol, were tested for potential effects against skin cancer. Phytochemical profile of *A. dracunculus* identified by PHPLC method [80].

#### Artemisia annua | Artemisinin

Melanoma is the primary cause of skin cancer-related deaths and one of the most aggressive and unpredictable tumours. Globally, there have been 4-6% annual increases in cases over the past decade. Artemisinin is a sesquiterpene lactone that is the main active ingredient of Artemisia annua and has received a Nobel Prize as an antimalarial agent [81]. Artemisinin was hypothesized to be an anticancer drug, and in vitro and in vivo studies supported this hypothesis. Based on the findings of Buommino et al., doses of 100 and 150 µM artemisinin caused a strong inhibition of the growth of A375M cells within 72 hours. Moreover, the chemotactic migration of human melanoma A375M cells was investigated as well as the inhibition mechanism. In consequence, artemisinin inhibits the production of metalloprotease 2 (MMP-2) and strongly inhibits the expression of  $\alpha v$  and  $\beta 3$  integrin subunits. A chemotherapeutic agent such as artemisinin may be effective against melanoma, based on the results of this study [82]. Additionally, there is another study where artemisinin was tested on uveal melanoma and found to be able to prevent metastasis. Throughout the results, artemisinin treatment inhibited uveal melanoma cell migration and invasion, and wound healing decreased in area in the initial knock and completely healed in subsequent knocks. Furthermore, a molecular pathway study of artemisinin showed that it inhibited PI3K, AKT, and mTOR phosphorylation signaling significantly in uveal melanoma cells. In an in vivo study, mice bearing subcutaneous uveal melanoma tumors did not lose weight and the tumors significantly shrank and grew less as a result of receiving artemisinin [83].

Cosmetics

#### Artemisia iwayomogi | Anti-Aging Effect

Artemisia iwayomogi is used in Korean traditional medicine for skin whitening, and its UV protection effect is scientifically proven. The whitening and anti-aging effects of A. iwayomogi were

assessed in vitro and in vivo. The study was conducted on five compounds obtained from the ethyl acetate and aqueous fractions. The compounds were tested in vitro to determine antioxidant activity by DPPH and ABTS, whitening effect through tyrosinase inhibition, and anti-wrinkle activity through elastase along with collagenase inhibition. Among isolated components, scopoletin and luteolin demonstrated significant antioxidant and whitening activities while scopolin, scopoletin and luteolin showed resistance to aging. The in vivo test involved preparing a cream containing the plant extract that contained a 1% aqueous solution. Twenty-one women with wrinkles who had just begun to develop wrinkles or already had wrinkles participated in the study for 8 weeks. *A. iwayomogi* water fraction significantly reduced wrinkles during the study period, indicating its anti-aging properties [84].

#### Artemisia argyi | Moisturizing Effect

Traditional medicine has used *Artemisia argyi* for treating skin problems, thus providing a basis for research into its properties. The study evaluated the moisturizing and antioxidant properties of *A. argyi* liquid essence, an aqueous solution obtained from the plant leaves through supercritical carbon dioxide extraction, and its mechanisms of action. The research was conducted on isoforms of hyaluronan synthase (HAS2 and HAS3), which responsible for synthesizing hyaluronic acid in the skin, and aquaporin 3 (AQP3) in HaCaT cells. Since, a lack of hyaluronic acid and aquaporins in the skin causes dehydration, which leads to the formation of folds and wrinkles. As result, treatment with liquid essence of *A. argyi* showed a significant increase the mRNA and protein expression of AQP3 and HAS2 indicating that it could be a key ingredient in cosmetics to address dry and aging skin problems [85,86].

### Determination of Tyrosinase Activity in *Artemisia* Species Germinating in Kazakhstan

Melanoma is among the most aggressive and malignant tumors in humans, originating from melanocytes and characterized by rapid proliferation and a high metastatic potential. Several factors contribute to its development, with UV radiation being the most prominent environmental risk factor. However, endogenous factors, such as hormonal imbalances—particularly those occurring during pregnancy—can also influence pigmentation changes and potentially contribute to melanoma progression. Additionally, individual variations in melanin synthesis, either increased or decreased, modulate the extent of UV-induced damage, leading to differential susceptibility among individuals.

Melanin synthesis, a key protective mechanism facilitating the human body's adaptation to environmental factors, is mediated by melanocytes [87–90]. These specialized cells contain highly organized, membrane-bound structures where melanin production occurs. However, with aging, physiological processes throughout the body, including melanin synthesis, gradually slow down and become less efficient. This decline leads to localized melanin accumulation in certain areas of the skin, which may contribute to an increased risk of melanoma development.

Tyrosinase, a copper-dependent enzyme, plays a pivotal role in regulating the rate of melanin biosynthesis. It catalyzes the oxidation of tyrosine to melanin and other related pigments through a series of enzymatic reactions. The inhibition of tyrosinase activity by specific inhibitors represents a viable approach for modulating melanin production, with potential applications in the treatment of hyperpigmentation disorders and other pigment-related conditions [91–93].

Several well-known tyrosinase inhibitors, including kojic acid, ascorbic acid, phytic acid, retinoic acid, arbutin, glabridine, and hydroquinone, have been widely studied for their depigmenting properties. However, their application is associated with various adverse effects. For instance, kojic acid has been reported to cause contact dermatitis and skin irritation, while arbutin can undergo conversion into hydroquinone, a compound with potential cytotoxicity. Hydroquinone itself is recognized for its toxic effects, raising concerns regarding its safety in long-term use. These limitations highlight the need for safer and more effective alternatives in melanin regulation.

The selection of appropriate treatment methods depends on various factors, including the specific condition and a comprehensive understanding of the underlying etiology of skin diseases, which is essential for determining optimal therapeutic strategies. Consequently, there is a growing need for the development of novel and safe treatment approaches. In this regard, natural bioactive compounds derived from plant sources native to Kazakhstan hold significant potential as effective and sustainable alternatives for dermatological applications.

In 2020, the Griffith Institute for Drug Discovery (Australia) conducted an analysis of tyrosinase content in the total extracts of 13 *Artemisia* plant species included in our study.

Melanocytes contain specialized, highly organized, membrane-bound structures where melanin biosynthesis occurs. With aging, overall physiological processes in the body gradually slow down and become less efficient. This decline similarly affects melanin synthesis, leading to its localized accumulation in certain areas of the skin, which may contribute to an increased risk of melanoma development. The findings of the study were as follows:

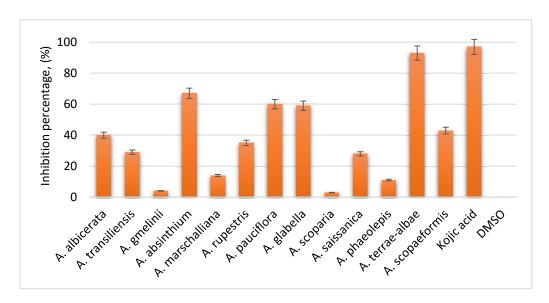


Figure 2. Tyrosinase content in plant extracts.

All samples were prepared in a 1% DMSO phosphate buffer, with a final extract concentration of 2.5 mg/mL. Kojic acid, at a concentration of 2.5 mg/mL, was used as a reference control due to its well-established efficacy as a potent tyrosinase inhibitor. Analysis of the results revealed that the total extracts of *A. terrae-albae* exhibited the highest tyrosinase inhibitory activity.

#### Conclusion

In conclusion, the ethnopharmacological importance of *Artemisia* species are both a reflection of traditional practices and a promising area for pharmacological research. The documentation of these traditional uses, combined with modern phytochemical analyzes, could lead to the development of effective dermatological treatments based on ancient wisdom. As noted in various studies, the integration of traditional knowledge with scientific methods improves our understanding of the true effectiveness of these species of vital plants. Moreover, in order to identify gaps in research field, the efficiency of medicinal plants that could be a candidate for new pharmaceuticals was researched by screening pharmacological and phytochemical studies.

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#### **Abbreviations**

The following abbreviations are used in this manuscript:

UV Ultraviolet

DNCB 2,4-dinitrochlorobenzene

MRSA Methicillin-resistant *Staphylococcus aureus*GC-MS Gas chromatography/mass spectrometry

PHPLC Preparative High Performance Liquid Chromatography

DMSO Dimethyl sulfoxide

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