

# PROSPECTS

## IN PHARMACEUTICAL SCIENCES

Prospects in Pharmaceutical Sciences, 23(4), 186-204  
<https://prospects.wum.edu.pl/>

Review

### COMPREHENSIVE REVIEW OF TOPICAL PHYTOFORMULATIONS AND PHARMACOLOGICAL ACTIVITIES FOR THE TREATMENT OF WRINKLES

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Received: 17.05.2025 / Revised: 14.07.2025 / Accepted: 17.07.2025 / Published in final version: 31.12.2025

#### ABSTRACT

The rising demand for natural cosmeceuticals is primarily attributed to their minimal side effects and their potential as alternatives to synthetic drugs. Numerous plant-derived compounds have been identified with properties beneficial for skin care, including whitening, anti-aging, and anti-wrinkle effects, as shown in the graphical abstract. This review comprehensively evaluates the efficacy of various herbal remedies for wrinkle treatment, drawing evidence from clinical studies, experimental research, and traditional practices. The study is aimed to identify medicinal plants with substantial scientific support for their therapeutic benefits, particularly in wrinkle reduction. An extensive literature search was conducted using databases such as PubMed, Google Scholar, Scopus, Web of Science, and ScienceDirect. The Plant List database was also consulted to confirm the scientific names, plant families, traditional uses, and active constituents of each plant. The analysis revealed 23 plant species from 19 different families that are traditionally used for managing symptoms of premature aging, including wrinkles and pimples. These plants were reviewed for their mechanisms of action, bioactive constituents, availability, and potential applications in cosmetic formulations. Scientific studies have confirmed that phytoconstituents possess anti-inflammatory, photoprotective, and anti-wrinkle properties, with proven inhibitory effects on wrinkle-related enzymes such as elastase and collagenase. Key botanicals such as *Diospyros kaki*, *Ipomoea carnea*, *Calendula officinalis*, *Ocimum basilicum*, and *Moringa oleifera* have shown significant cosmeceutical potential. Overall, the findings suggest that phytoconstituents from medicinal plants represent promising and potentially superior alternatives to synthetic agents for the development of effective anti-wrinkle treatments.

**KEYWORDS:** anti-wrinkles, pharmacological activity, traditional plants, collagen, elastin.

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#### 1. Introduction

The human body's largest organ is the skin, which serves three vital roles: protecting the body from outside threats, acting as a thermostat, and assisting with sensory feedback. The major sign of aging skin, which appears visibly as wrinkles, develops as a result of chronological aging and environmental exposures. The factors behind intrinsic aging are influenced by genetic factors, hormonal changes, metabolic processes, and oxidative stress imbalance. In contrast, extrinsic aging is primarily caused by UV radiation and pollution, which are exacerbated by smoking habits, inadequate nutrition, and stress exposure. UVB radiation, in particular, functions as the primary environmental factor in skin aging because it produces reactive oxygen species that cause oxidative stress, coupled with tissue inflammation and degradation of the collagen and elastin matrix [1],[2].

Oxidative stress activates the production of inflammatory cytokines and matrix metalloproteinases (MMPs), resulting in collagen fiber breakdown, reduced skin elasticity, and wrinkle formation. Skin structure and resilience are impaired because fibroblasts malfunction and reduce their production of glycosaminoglycans (GAGs) and proteoglycans (PGs). Chronic molecular and cellular changes in skin tissue result in fine wrinkles, accompanied by deep wrinkles, decreased skin stiffness, and reduced elasticity [3].

Standard methods of anti-aging therapy, which combine chemical treatments with lasers and synthetic topical medications, demonstrate some benefits but also produce negative effects and high costs, offering a limited long-term impact [4],[5]. New interest continues to grow regarding the development and implementation of natural, safer, and

more effective treatment solutions [6],[7].

Phytoformulations obtained from plant sources show promise as medical treatments that support both wrinkle prevention and treatment. The skin-rejuvenating properties, anti-collagenase, and anti-inflammatory effects, along with the antioxidant properties of flavonoids, polyphenols, terpenoids, and alkaloids, make these phytochemicals highly potent. The natural compounds demonstrate multiple health benefits, which include stress reduction and MMP inhibition as well as collagen stimulation and overall skin health maintenance [8],[9].

Recently, consumer preference has shifted markedly toward natural and plant-based cosmeceuticals, driven by concerns about the detrimental effects and long-term safety of synthetic substances. Natural products are frequently regarded as safer, more biocompatible, and environmentally sustainable alternatives. This transition has led to an increasing interest in herbal formulations for dermatological purposes, particularly in combating signs of skin aging, including wrinkles, fine lines, and reduced elasticity [10]. Skin aging is a complex biological process affected by intrinsic factors (genetic and chronological aging) and extrinsic factors (environmental influences such as UV radiation, pollution, and lifestyle choices). Wrinkles, a significant indicator of aging, are primarily attributed to the deterioration of dermal structural proteins, including collagen and elastin, which are frequently facilitated by enzymes such as collagenase and elastase [11]. Research indicates that oxidative stress and chronic inflammation intensify these effects, hastening skin aging [12]. *Ocimum basilicum* exhibits anti-inflammatory and antioxidant qualities that are good for skin health [13], while *Calendula officinalis* has been shown to encourage collagen synthesis. Similarly, *in vitro* and *in vivo* studies have shown that *Moringa oleifera* and *Diospyros kaki* have anti-wrinkle and UV-protective properties [14],[15].

The objective of this review is to present a comprehensive analysis of several studies conducted in relation to anti-wrinkle formulations that include natural components, employing a literature study technique. It is expected that this review will provide an in-depth understanding of the most recent advancements in this area and serve as a solid foundation for future research on more effective cosmetics and novel anti-wrinkle skin care products. To prevent data duplication, three reviewers separately extracted the data before the final paper selection was made.

In addition to exploring new cosmetic compounds, extensive research is being conducted to increase the bioavailability of cosmetic products. This emphasis stems from the fact that many phytoconstituents, although they have been shown to have pharmacological potential, do not always penetrate the skin well or remain stable when applied topically. To address these issues, researchers are exploring advanced formulation techniques, including nanoemulsions, liposomes, solid lipid nanoparticles, and other carrier systems, to enhance the efficacy of active substances and facilitate their targeted delivery. These new methods not only make phytoformulations more potent in treating skin problems, but they also help make topical therapies for wrinkles and other symptoms of skin aging safer and more effective.

This review highlights the significant potential of medicinal plants and their phytoconstituents in the treatment of wrinkles and skin aging. They are effective natural substitutes for synthetic agents due to their anti-inflammatory, antioxidant, and enzyme-inhibitory qualities, which are supported by scientific evidence. Using these botanicals in topical formulations presents a viable strategy for creating anti-wrinkle cosmeceuticals that are both safe and effective.

### 1.1. Factors involved in the development of wrinkles

One of the most obvious and early signs of skin aging is the appearance of wrinkles, which are caused by a complex interaction between extrinsic and intrinsic factors [16]. While the complete pathophysiology of wrinkle formation remains to be fully elucidated, research indicates that nearly 90% of wrinkles are attributed to prolonged and unprotected exposure to ultraviolet (UV) radiation, commonly known as photoaging. Excessive reactive oxygen species (ROS) produced by UV rays penetrating the skin cause oxidative stress (OxS), a major cause of skin aging.

Pro-inflammatory cytokines, such as interleukins (ILs) and tumor necrosis factor-alpha (TNF- $\alpha$ ), are upregulated as a result of ROS-induced oxidative stress. Matrix metalloproteinases (MMPs), specifically MMP-1, MMP-3, and MMP-9, are activated by these inflammatory mediators and break down key structural proteins in the extracellular matrix (ECM), particularly collagen and elastin. As these ECM components gradually degrade, the skin loses its elasticity, hydration, and structural integrity, which eventually leads to the appearance of deep wrinkles and fine lines, as shown in Fig. 1 [17].

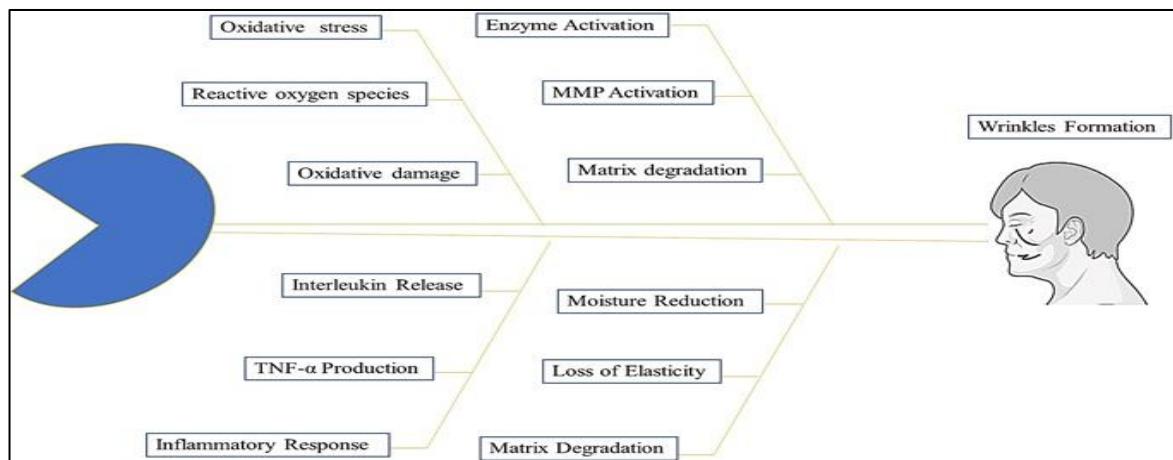


Fig. 1. Understanding the formation of skin aging [18].

Several external lifestyle and environmental factors, in addition to UV exposure, significantly accelerate the development of wrinkles. These include poor skin care practices, pollution in the environment, poor eating habits, and tobacco use, which is particularly linked to smoker's wrinkles, which are characterized by deep perioral lines and dry, lifeless skin. Smoking accelerates the aging process by increasing oxidative stress, reducing skin perfusion, and impairing collagen production.

Effective anti-wrinkle treatments must therefore take a multifactorial approach, combining substances that inhibit MMP activity and lower the mRNA expression of ILs and MMPs with antioxidant and anti-inflammatory agents. In order to prevent or lessen wrinkles comprehensively, strategies must also take into account sun protection, pollution shielding, lifestyle changes, and nutritional support [19], [2].

### 1.2. Anti-wrinkle approaches to prevent wrinkles

Tomas et al. (2025) demonstrated that inhibiting inflammation is an effective approach for slowing the signs of aging. The herbal extract can restrict or minimize ROS generation by suppressing MMP-2 activity, along with a consequent increase in collagen production [20]. Furthermore, in this review, herbal formulations were found to have anti-wrinkle properties. Many plant extracts have demonstrated anti-wrinkle efficacy through antioxidant mechanisms. Numerous studies have demonstrated that these extracts exhibit antioxidant activity, which is also utilized as an anti-inflammatory agent and for inhibiting collagenase and elastase, thereby resulting in superior anti-wrinkle properties. Another study showed superoxide-scavenging activity as a wrinkle-prevention strategy [20]. New treatment strategies are being investigated to avoid the production of reactive oxygen species, which can cause skin damage due to atmospheric factors. Sunscreens are another option for shielding the skin from UV radiation.

### 1.3. Importance of phytoconstituents in cosmeceuticals for treating wrinkles

Synthetic substances are commonly used as key components in cosmetic products; however, there has been a recent trend towards incorporating various natural compounds as primary active ingredients in cosmetology. The discovery and utilization of new natural sources and their extracts in cosmetics and cosmeceuticals have drawn attention in the skincare industry recently. Cosmetics have been used to maintain skin health and hygiene since ancient times. However, the modern concept of using cosmetics encompasses not only keeping skin healthy but also treating various skin-related conditions and slowing down the aging process. The pharmacologically active components of many medicinal plants, including alkaloids, lignin, tannins, terpenoids, polyphenols, and flavonoids, which are generally referred to as phytochemicals, are thought to have positive benefits for skin health. Herbal extracts have been used much more frequently in the past few decades [21]. Phytochemical compounds derived from plants have garnered the interest of both scientists and the general public due to their ability to enhance both the quantity and quality of life [22].

### 1.4. Need for natural anti-wrinkle topically applied formulations

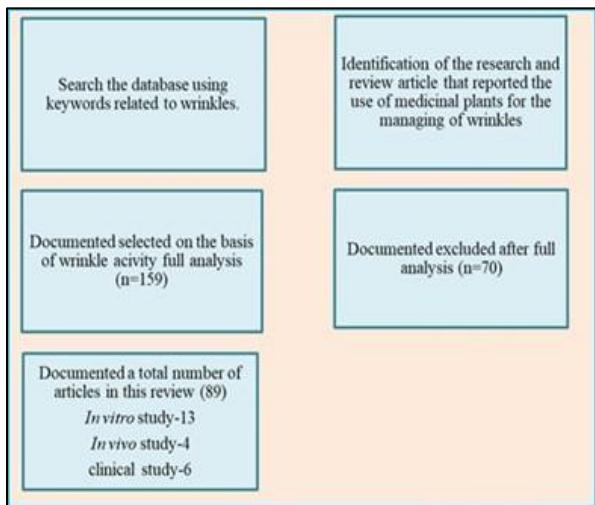
The topical route has several benefits over other routes, including continuous medication or phytoconstituent delivery, fewer side effects, improved patient compliance, and avoidance of hepatic first-pass effects [23]. Although the stratum corneum serves as the skin's primary barrier, it also prevents dehydration and hinders the absorption of many medications. The stratum corneum's intercellular lipids are essential for creating the skin's permeability barrier. Researchers are currently developing skin treatments that remain primarily on the surface and do not penetrate the body, targeting the stratum corneum, viable epidermis, and skin appendages [24]. Researchers have observed that topical tretinoin and isotretinoin reduce the roughness, sallowness, and coarse and fine wrinkles associated with photoaging [25]. Topical sunscreen application is the suggested strategy for successfully reducing UV radiation exposure and the risk of sunburn on the skin [26]. Reducing the activity of free radicals is one of the many strategies to stop the aging process of the skin. Antioxidants are substances that can be utilized to stop the activity of free radicals [27]. Polyphenols, flavonoids, and phenolic acids found in plants and marine algae have been generally shown to possess anti-aging properties, including antioxidant activity and anti-wrinkle effects [28]. Specific methods employ topically applied agents that penetrate the cutaneous tissues to protect and heal them from the inside out, including anti-aging, antioxidant, anti-wrinkle, and anti-inflammatory components [29].

## 2. Materials and Methods

The following electronic databases were used in this review: PubMed, Google Scholar, Web of Science, and Scopus. The search strategy used the following terms: "anti-wrinkles AND phytoconstituents AND formulation", "medicinal plants AND antioxidant AND ROS inhibition", "traditional uses AND wrinkles AND collagenase inhibition", and "elastase inhibition AND medicinal plants AND anti-wrinkles", and "botanical extract AND anti-wrinkles". This strategy was employed to gather relevant data from numerous research studies on various anti-wrinkle formulations and the application of natural compounds with anti-wrinkle properties. The purpose of this review is to help researchers better understand the current context and findings, so that they may serve as a strong basis for future research. Only national and international journals that were significantly related to the research topic were included in this study due to its extremely selective inclusion criteria. To assure the currentness of the material provided, we have incorporated articles that were published between 2009 and 2023, or during the last fifteen years.

### 2.1. Data screening and categorization of information

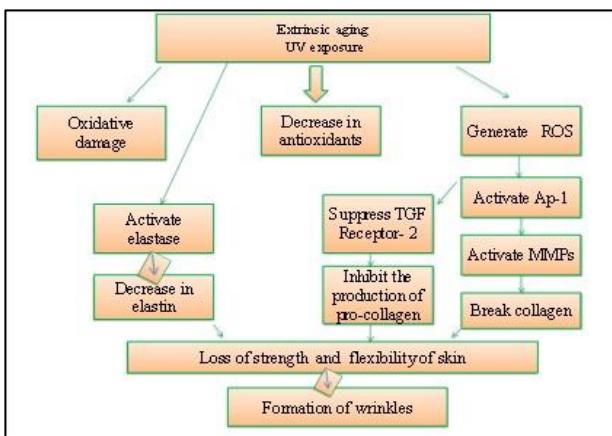
After identifying research and review papers discussing the application of medicinal plants in the treatment of wrinkles, 159 scientific articles were selected from the database. Subsequently, a total of 70 documents were excluded that did not meet the criteria for this review, as shown in Fig. 2. Finally, 89 articles were chosen that contained data on the use of anti-wrinkle agents.



**Fig. 2.** Diagram showing process scheme used to select scientific papers for this review.

### 3. Results

Numerous processes, including OxS, inflammation, changes in the extracellular matrix, and a decline in skin cell renewal, contribute to skin aging [29]. Collagenase and elastase are specific types of MMPs that target collagen and elastin. A naturally occurring glycosaminoglycan called hyaluronic acid (HA) supports the hydration and flexibility of the skin [30]. This results in reduced levels of fibers and collagen type VII (Col-7), which compromises the bond between the epidermis and dermis, resulting in skin that appears aged. The aging of the skin involves various changes caused by both internal factors (such as how our cells function, genetic changes, and hormonal fluctuations) and external factors (including pollution, chemicals, UV rays, and toxins). UVB radiation promotes the generation of ROS. Long-term exposure to UV radiation typically leads to an increase in ECM degradation. UV radiation can activate an enzyme called matrix metalloproteinase, which is responsible for breaking down components of the ECM, such as collagen and elastin. However, if the skin is subjected to photoaging stress, the accumulation of ROS can indirectly activate skin enzymes that break down collagen and elastin, such as collagenase and elastase. Thus, the production of collagenase and elastase stimulates early skin aging, which looks like deep furrows, freckles, sallowness, and wrinkles, as shown in Fig. 3. Fibroblasts and proteins, such as collagen and elastin, make up the extracellular matrix (ECM), the skin's supporting

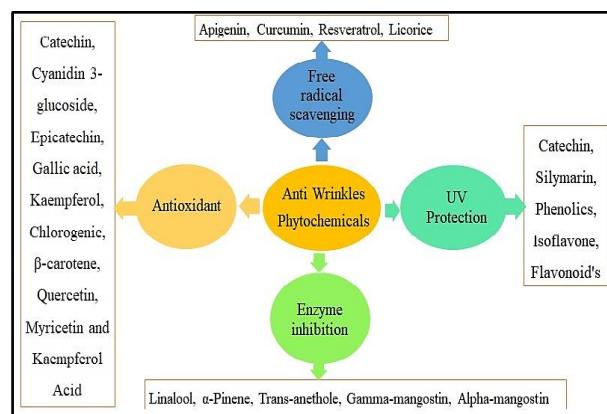


**Fig. 3.** Molecular mechanism behind wrinkles.

layer. The most prevalent protein structure in the human dermis layer, collagen, gives the skin its tensile strength. However, elastin, a network of fibers found in connective tissue, provides the skin with its elastic recoil characteristic. Elastin and collagen are vital for the skin, playing a critical role in preserving its elasticity, plumpness, integrity, flexibility, and youthful appearance [5].

#### 3.1. Free radicals' role in the formation of wrinkles

Metabolic processes within cells continuously generate ROS. However, excessive accumulation of these species may result in OxS and damage various biological components, such as lipids, proteins, and DNA. Herman's theory of aging, the free radical theory, posits that free radicals derived from oxygen are responsible for age-related damage. This theory has historically been one of the most widely accepted and popular explanations for the aging process. The theoretical framework commonly referred to as the "OxS theory of aging" is centered on the role of ROS, which is known to generate oxidative stress. This theory posits that both free radicals and non-radical ROS play crucial roles in the aging process. The thickening of the outer skin layer mainly leads to wrinkles, and ROS can significantly contribute to the formation of wrinkles by promoting the release of MMP and pro-inflammatory cytokines, while also breaking down extracellular matrix proteins. Exposure to UV radiation greatly accelerates the skin aging process [31]. Photo-oxidative stress in the skin induced by reactive oxygen species from sun radiation is considered the principal pathogenic process that destroys extracellular matrix proteins, leading to wrinkle formation. Additionally, OxS can increase the production of elastin mRNA in skin cells, resulting in changes to the skin that make it less elastic when exposed to UVR. Additionally, OxS causes dryness, elasticity loss, and an increase in wrinkles [32].



isoflavone, flavonoids, linalool,  $\alpha$ -pinene, trans-anethole, gamma-mangostin, and alpha-mangostin. The steps for their prevention can be understood with the help of Fig. 4. Several phytoconstituents have been chosen, and their comprehensive profiles have been supplied. Table 1 illustrates the mechanism of action of phytoconstituents when applied topically, and their chemical compound shown

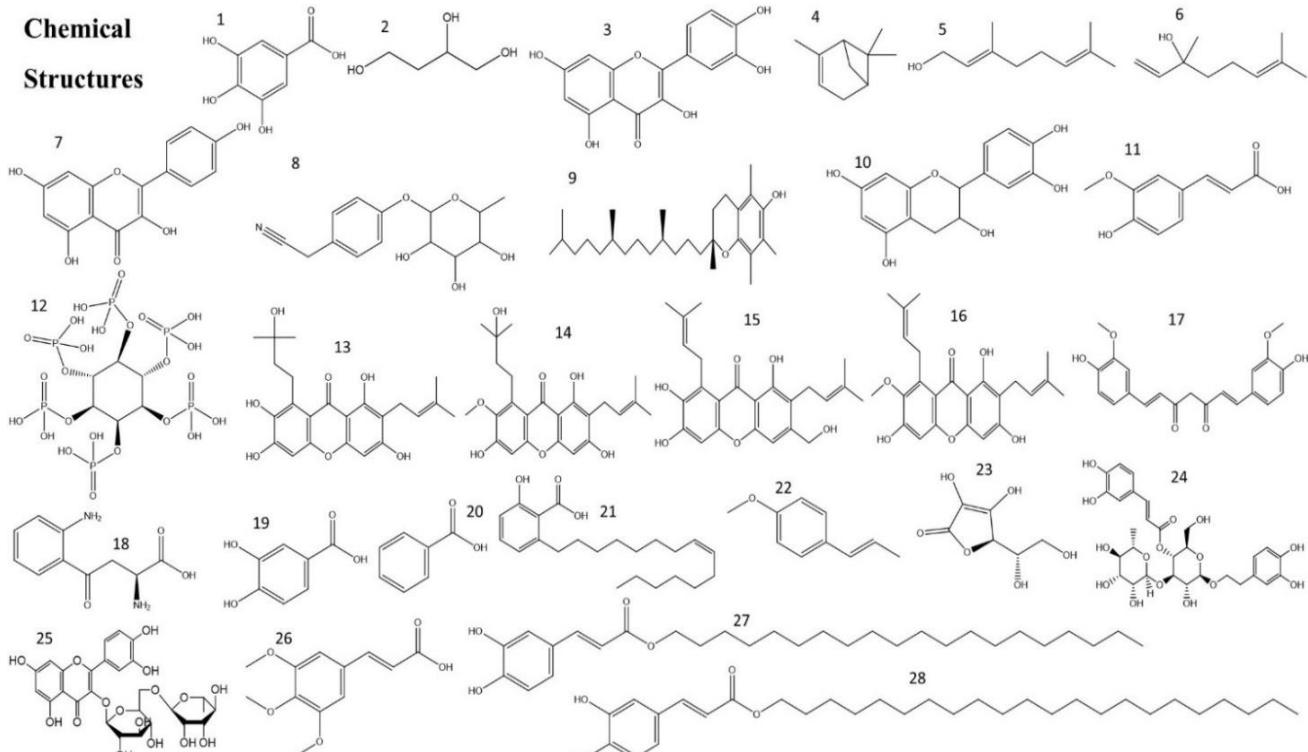
in Fig. 5. [31]. Facial wrinkles, particularly in the mouth or eyes, are a significant concern for maintaining a youthful appearance. Phytoextracts, rich in bioactive components, are more effective in wrinkle treatment and have fewer side effects than many synthetic anti-wrinkle chemicals, making them widely used in topical formulations due to their antioxidant and anti-wrinkle properties.

**Table 1.** Phytoextract-based formulations with mechanisms of action to prevent wrinkles.

Sr. no.	Plant name (Botanical name)	Family	Plant's part used	Active (Phytoconstituents)	Therapeutic use	Type of formulation	Mechanism of action	Ref.
01	<i>Diospyros kaki</i> L. (Persimmon Fruits)	<i>Ebenaceae</i>	Fruit	Uronic acid Galacturonic acid p-Coumaric acid Ferulic acid Gallic acid (Fig.5, compound 1)	Anti-wrinkle	Emulgel	Antioxidant activity Elastase, collagenase enzymes inhibitory activities	[32]
02	<i>Ipomoea carnea</i> (Bush Morning Glory)	<i>Convolvulaceae</i>	leaves	1,2,4-Butanetriol (Fig. 5, compound 2)	Anti-wrinkle	Cream	Antioxidant activity Inhibition of UVB radiation Enhances the level of protein content Increases the level of superoxide dismutase and catalase activity	[25], [33]
03	<i>Calendula officinalis</i> (marigold)	<i>Compositae</i>	Flowers	Flavonoids - quercetin (Fig. 5, compound 3) Rutin Glycosides of sesquiterpene and triterpenes Essential oil - $\alpha$ -pinene (Fig. 5, compound 4) Sabinene Geraniol (Fig. 5, compound 5)	Anti-wrinkle	Cream	Anti-inflammatory properties Resists the absorption of UVB radiation Antioxidant activity	[34], [35]
04	<i>Ocimum basilicum</i> L. (basil)	<i>Lamiaceae</i>	Leaves	Linalool (Fig. 5, compound 6)	Anti-wrinkle	Cream	The DPPH free radical scavenging method is employed to assess antioxidant activity	[36], [6]
05	<i>Moringa oleifera</i> (drum stick)	<i>Moringaceae</i>	Seeds	Kaempferol (Fig. 5, compound 7) Quercetin Moringinie Niazirin (Fig. 5, compound 8) Niazinine A	Anti-wrinkle Fine lines	Cream	Inhibits the loss of elastin and collagen Makes the skin look younger by rejuvenating skin photo-damage Antioxidant	[37], [38]
06	<i>Helianthus annuus</i> (sunflower)	<i>Asteraceae</i>	Seeds	Alpha-tocopherol (Fig. 5, compound 9)	Anti-wrinkle	Cream	Absorbs UV rays Antioxidant	[40], [41], [42]
07	<i>Coriandrum sativum</i> (coriander)	<i>Apiaceae</i>	Seeds	Linalool Alpha Pinene	Anti-wrinkle Anti-inflammatory	Lipid Nanoparticles	Inhibition of collagenase, elastase and hyaluronidase	[43], [44]
08	<i>Punica granatum</i> (pomegranate)	<i>Lythraceae</i>	Peel	Flavonoids, Polyphenols Catechin (Fig. 5, compound 10) quercetin ellagitannin epicatechin gallotannin	Anti-wrinkle	Cream	Stimulates the collagen production Anti-elastase activity Prevents ultraviolet radiation Antioxidant Absorbs the UV rays	[45], [46], [47]

09	<i>Tagetes erecta L</i> (marigold)	Asteraceae	Flowers	Flavonoids -quercetin	Anti-wrinkle	Nanoemulsion	Antioxidant DPPH, reducing power Superoxide radical scavenging activity.	[48]
10	<i>Oryza sativa</i> (Rice bran)	Poaceae	Seeds (Rice husks)	$\gamma$ -Oryzanol Ferulic acid (Fig. 5, compound 11) Phytic acid (Fig. 5, compound 12)	Anti-wrinkle	Nanoemulsion	Antioxidant Stimulating human fibroblast growth MMP-2 Inhibition Protection from UV radiation	[49], [50], [51]
11	<i>Azadirachta indica</i> (neem)	Meliaceae	Seed, leaf	Catechin Phenols Gallic acid	Anti-wrinkle	Cream	Antioxidant Increases type I elastin and procollagen Inhibits DPPH	[52], [53]
12	<i>Garcinia mangostana</i> (mangosteen)	Clusiaceae	Peel	Garcinone C (Fig. 5, compound 13) Garcinone D (Fig. 5, compound 14) Gamma-mangostin (Fig. 5, compound 15) Alpha-mangostin (Fig. 5, compound 16)	Anti-wrinkle	Cream	Antioxidant DPPH, ABTS, ferric reducing Hydroperoxide scavenging Enzymatic activity: anti-hyaluronidase, anti-elastase, and anti-collagenase	[54], [55]
13	<i>Curcuma longa</i> (turmeric)	Zingiberaceae	Rhizomes	Curcumin (Fig. 5, compound 17)	Photoprotection Anti-inflammatory	Cream	Inhibits reactive oxygen species, an antioxidant	[56]
14	<i>Ginkgo biloba L.</i> (ginkgo)	Ginkgoaceae	Leaves	Kynurenic acid (Fig. 5, compound 18) Protocatechuic acid (Fig. 5, compound 19) p-Hydroxy Gallic acid Benzoic acid (Fig. 5, compound 20) Ginkgolic acid (Fig. 5, compound 21)	Anti-wrinkles	Cream	Inhibits free radicals Antioxidant Anti-photo-damages Increased collagen degradation Decreased MMP-1 expression	[57]
15	<i>Clausena harmandiana</i> (Song Fa)	Rutaceae	Leaves	trans-Anethole (Fig. 5, compound 22)	Anti-wrinkle	Microemulsion	Enzymatic activity of anti-collagenase, elastase	[58]
16	<i>Silybum marianum L.</i> (cardus marianus, milk thistle)	Asteraceae	Fruit	Silymarin Silybin a and b Isosilybin a and b Silychristin and Isosilychristin Silydiamin	Anti-wrinkle	Cream	Inhibition of ROS Increase in elasticity.	[59], [60], [61]
17	<i>Acmella oleracea</i> (L.) (toothache plant)	Asteraceae	Roots and aerial part of the plant	Spilanthol	Anti-wrinkles Anti-inflammatory	Emulsion	Antioxidant inhibits facial muscle contractions	[62], [63]
18	<i>Citrus reticulata</i> Blanco (Tangerine)	Rutaceae	Peel	Phenolic Flavonoids	Anti-wrinkle	Cream	Enzymatic activity: Anti-collagenase and anti-elastase Antioxidant.	[64]
19	<i>Solanum lycopersicum</i> Mill. (tomatoes)	Solanaceae	Fruit	Polyphenols Vitamin C (Fig. 5, compound 23) Lycopene	Anti-wrinkle	Cream	Antioxidant Inhibition of free radical damage In vitro elastase inhibitory assay.	[65], [66]
20	<i>Veronica officinalis</i> (speedwell)	Plantaginaceae	whole plant	Verbascoside (Fig. 5, compound 24)	Anti-wrinkle	Cream		[67]

21	<i>Anacardium occidentale L</i> (cashew Tree)	Anacardiaceae	Leaves	Flavonoid-quercetin Phenolic compounds- chlorogenic acid Rutin (Fig. 5, compound 25)	Anti-wrinkle	Cream	Anti-Collagenase Inhibition of Reactive oxygen species	[68], [69]
22	<i>Isatis indigotica</i>	Cruciferae	Leaves	3,4,5- Trimethoxycinnamic acid (Fig. 5, compound 26)	Anti-wrinkle Anti-inflammatory	Cream	Suppression of the expression of the pro-inflammatory cytokine IL-8 mRNA and MMP-1 and MMP-3 Antioxidant	[2]
23	<i>Glycyrrhiza glabra</i> (licorice)	Leguminosae (also known as Fabaceae)	Root	Eicosanyl caffeoate Fig. 5, compound 27, Docosyl caffeoate Fig. 5, compound 28	Anti-wrinkle	Cream	Antioxidant Inhibition of elastase and matrix metalloproteinase- 1, Collagenase Inhibitory Assay Photoprotection.	[70], [20]



**Fig. 5.** Chemical compounds with anti-wrinkle potential isolated from traditional plants are named as 1. Gallic acid, 2. 1,2,4-butanetriol, 3. Quercetin, 4. Alpha-pinene, 5. Geraniol, 6. Linalool, 7. Kaempferol, 8. Niazirin, 9. Alpha-tocopherol, 10. Catechin, 11. Ferulic acid, 12. phytic acid, 13. Garcinone C, 14. Garcinone D, 15. Gamma-mangostin, 16. Alpha-mangostin, 17. Curcumin, 18. kynurenic acid, 19. Protocatechuic acid, 20. Benzoic acid, 21. Ginkgolic acid, 22. Trans-anethole, 23. Vitamin C, 24. Verbascoside, 25. Rutin, 26. 3,4,5-trimethoxycinnamic acid, 27. Eicosanyl caffeoate, 28. Docosyl caffeoate.

### 3.2.1. *Diospyros kaki* L.

Persimmon (*Diospyros kaki*) is a well-known and widely grown fruit in the Ebenaceae family. Its pulp contains ferulic acid, p-coumaric acid, gallic acid, and several bioactive polyphenols. Additionally, carotenoids, including cis-mutatoxanthin, antheraxanthin, zeaxanthin, neolutein, cryptoxanthins,  $\alpha$ -carotene,  $\beta$ -carotene, and fatty acid

esters of  $\beta$ -cryptoxanthin, are noted. Persimmons are known to possess several physiological qualities, including antioxidant activity, due to these active components. However, few studies have examined the pharmacological effects of persimmon's high-molecular-weight components, especially polysaccharides. It has been demonstrated that polysaccharides extracted from persimmon fruit and leaves possess medicinal properties, including antioxidant

activity. Human dermal fibroblasts were used to evaluate the anti-wrinkle properties of the test sample. The assay verified that the anti-wrinkle activity assessment concentrations were not cytotoxic. Numerous medicinally active substances, including organic acids, polyphenols, flavonoids, terpenoids, and polysaccharides, are found in persimmon. Persimmon fruit pulp showed antioxidant and elastase, collagenase enzymes inhibitory activities [33].

### 3.2.2. *Ipomoea carnea*

*Ipomoea carnea* herbal cream (FIHC) at 50 and 100 mg dosages did not significantly alter the reversal of UVB damage as observed in the preceding weeks. FIHC cream at a high dose of 200 mg was sufficient to minimize UVB-induced damage to the dorsal skin surface (G6). The research found that the extract from *I. carnea* leaves has significant antioxidant properties, which can help prevent premature skin aging and cellular damage. In this study, a herbal cream was prepared and showed protection against UVB radiation-induced skin burns. The cream demonstrated a consistent and effective ameliorative effect on skin burns induced by UVB radiation, with its efficacy increasing alongside higher concentrations of the extract. The cream also maintained the levels of certain enzymes and other substances after treating skin damaged by UVB, indicating that it can help mitigate the harm caused by UVB. The cream was tested on rats exposed to UVB radiation and was found to reduce sunburn significantly.

### 3.2.3. *Calendula officinalis*

*Calendula* is a member of the composite family and contains a significant amount of saponins, volatile essential oils, and other compounds. It can protect the skin from UV rays. Its properties have increased interest in the use of this material in the cosmetic sector [71]. This study showed the potential of calendula essential oil as an antioxidant in skin care treatments that can minimize or prevent OxS, and slow down the wrinkling process [35]. Bioactive and free radical-scavenging substances found in calendula extract can interact with ROS to either eliminate them or reduce their harmful effects. Alpha-tocopherol, ascorbic acid, vitamin E, vitamin C, quercetin, beta-carotene, and amino acids are examples of these bioactive substances, also known as antioxidants [72]. It was found that the calendula essential oil-loaded formulation could induce skin tightness, which prevents skin damage and delays the aging process, including the development of wrinkles. They also showed improvements in some elastic and viscoelastic parameters. Carotenoids and other components present in calendula extract may be responsible for the significant increase in viscoelasticity, glycosides of sesquiterpenes, saponins, triterpenes, flavonoids, etc. [73].

### 3.2.4. *Ocimum basilicum*

*Ocimum basilicum* cream was formulated to treat acne vulgaris, a common disorder impacting both adults and children. Anti-acne lotions derived from crude plant extracts have traditionally been employed for their antibacterial and antioxidant properties to alleviate inflammation associated with acneiform signs [74]. All parts of this plant, from the roots to the seeds, have various medical properties. *Ocimum basilicum* exhibits anti-aging and antioxidant properties, and can help remove dead skin cells [75]. The antioxidant capacity of *O. basilicum* essential

oil was assessed. The essential oil demonstrated anti-wrinkle benefits when evaluated for antioxidant activity via DPPH free radical scavenging [37].

### 3.2.5. *Moringa oleifera*

The *Moringa oleifera* seed oil contains a high antioxidant content. A nanoemulsion of *Moringa oleifera* seed oil was formulated and demonstrated efficacy as an anti-wrinkle treatment upon direct application to human skin. Due to their small droplet size (less than 100 nm), it was claimed that the W/O nanoemulsion of *M. oleifera* was efficiently dispersed and delivered via the stratum corneum. The antioxidative effect of *M. oleifera* seed oil nanoemulsions can prevent the loss of elastin and collagen. It was found that it could protect against UV radiation. The candidate appeared older because of changes in skin physiology. Although there are many different treatment options, the easiest way to achieve this is by applying anti-wrinkle formulations, which help renew the skin and make it look younger, by preventing or restoring fine lines and wrinkles. The anti-wrinkle properties of *Moringa oleifera* are linked to the high concentration of antioxidants in the seed oil.

### 3.2.6. *Helianthus annuus* L.

Sunflowers belong to the Asteraceae family, which contains compounds that act as a sunscreen ingredient. Vitamin E functions as a natural sunscreen, which is a main component found in sunflower oil. Vitamin E, or alpha-tocopherol, acts as an antioxidant and provides UV protection in cosmetics [40]. Excessive UV radiation commonly causes skin inflammation and photoaging. Reactive oxygen species (ROS) produced by UV radiation are a primary cause of photo-damage, which results in wrinkles. Increased enzyme levels, such as elastase and collagenase, break down elastin and collagen. *Helianthus annuus* L. flowers (HAF) have been shown to possess significant antioxidant and anti-inflammatory properties. HAF extract markedly suppressed UVB-induced reactive oxygen species and matrix metalloproteinase (MMP-1 and MMP-3) synthesis, concurrently diminishing procollagen type I levels. Subsequent research revealed that the inhibitory effects on photoaging were associated with the promotion of nuclear translocation of nuclear factor erythroid 2-related factor 2 (Nrf2), an increase in transforming growth factor (TGF- $\beta$ 1) levels, and a decrease in the phosphorylation of activating protein (AP-1) and mitogen-activated protein kinase (MAPK) [42].

### 3.2.7. *Coriandrum sativum*

*Coriandrum sativum* has numerous biological benefits and an attractive fragrance, and its main constituent is linalool, which has shown anti-wrinkle activity and has been used for skin care for decades [43]. *Coriandrum sativum* L. seeds are utilized worldwide to combat inflammation and the production of reactive oxygen species (ROS). An analysis of the polyphenol concentration in *Coriandrum sativum* seeds showed potential anti-inflammatory and antioxidant characteristics [76]. Jeya et al. (2019) investigated the antimicrobial and antioxidant properties of coriander essential oil. The essential oil of *Coriandrum sativum* L. seeds demonstrated exceptional antioxidant activity. Antioxidants help slow down the aging process [77].

### 3.2.8. *Punica granatum* L.

Pomegranate peel and seeds have both been found to contain antioxidant properties that may be used to shield the skin from UV ray damage. UV radiation is a major source of ROS, Oxs, DNA damage, and an increase in skin aging [78]. Using natural antioxidants topically, including polyphenols, is effective in preventing UV-induced Oxs and skin abnormalities. These compounds can absorb ultraviolet radiation before it penetrates the epidermis and dermis. The formulation of topical dosage forms for the administration of pomegranate antioxidant components to deeper skin layers was found to be advantageous for preserving the skin against UV radiation [79]. Due to their ability to enhance the penetration of medications through the skin and thereby increase the topical effect, nanoemulsions have been considered promising drug carriers for treating skin issues [80].

### 3.2.9. *Tagetes erecta* L.

*Tagetes erecta* L., or marigold flower, belongs to the Asteraceae family. The antioxidant activity (DPPH assay) of the gel-containing nanoemulsion loaded with ethyl acetate (EANG) was examined before and after three months of storage under various conditions. The results showed the EANG's physical stability and its capacity to maintain good antioxidant activity across various storage environments. It showed a noticeable reduction in all wrinkle parameters. The results strongly indicated that the gel comprising a nanoemulsion with marigold flower extract was a possible anti-wrinkle cosmetic. MMPs are zinc-dependent endopeptidases. MMP-1 (interstitial collagenase) degrades collagen type I, while MMP-2 also degrades elastin and basement membrane components, including collagen types IV and VII. MMP-1 largely regulates the degradation of dermal collagen, whereas MMP-2 and MMP-9 degrade extracellular matrix proteins that contribute to wrinkles and skin thickness [81]. This study demonstrated that the gel with nanoemulsion loaded with EA was stable under various storage conditions and exhibited greater stability than EA alone in the gel. It showed high antioxidant activity and excellent stability. Therefore, the EANG could aid in delivering the active compound into the skin, which is beneficial for cosmetic applications. The clinical evaluation revealed that the gel containing nanoemulsions loaded with EA could enhance skin hydration after treatment. It also reduced skin wrinkles compared to untreated and placebo areas. Furthermore, it showed no skin irritation throughout the study. The results also revealed that the antioxidant capacity of EA plays an important role in reducing skin wrinkles. Moreover, loading EA into a nanoemulsion demonstrated better stability and efficiency, positioning it as a promising anti-aging cosmeceutical product [82].

### 3.2.10. *Oryza sativa*

Rice bran oil is used in the cosmetic sector in sunscreen formulas (protecting against UVR) and in anti-aging products, as well as for treating skin problems. Rice bran oil nanoemulsions were prepared using simple mixing methods to assess their stability, potential irritancy, and moisturizing properties in individuals with both healthy and unhealthy skin. The nanoemulsion was prepared by a phase diagram method with 10% surfactant, sorbita noleate/PEG-30 castor oil, 10% rice bran oil, 0.50% preservative, and 0.05% antioxidant in distilled water. During this study, the nanoemulsion remained stable. In lab tests, this

formulation showed very little irritation, and when applied to human skin, the nanoemulsion helped maintain skin hydration. Rice bran oil bark aqueous extract has traditionally been used in sunscreen formulas, anti-aging products, and the treatment of skin problems.

### 3.2.11. *Azadirachta indica*

Rinaldi et al. prepared nanoemulsions of neem seed oil (which is high in bioactive ingredients) and Tween 20 as a non-ionic surfactant, modifying the oil/surfactant ratio; a mean droplet size between 10 and 100 nm was achieved. Significant antioxidant activity has been reported [83]. Neem has been utilized in India for decades to treat dermatological issues. The study investigated the anti-aging properties of neem leaf extract at concentrations of 1, 10, and 50 mg/mL on the skin of hairless mice exposed to UVB radiation. Neem leaf extracts enhanced type I procollagen and elastin production in a UVB-irradiated skin model. It has been demonstrated that treating signs of aging skin, such as wrinkles, thickness, water loss, and erythema, with UVB radiation on hairless mice was quite effective. Consequently, the data indicate that neem leaf ethanolic extract possesses significant anti-aging potential for topical medical applications [53].

### 3.2.12. *Garcinia mangostana* L.

This formula utilizes mangosteen peel, a waste product, to reduce waste generation. The mangosteen creams were formulated with natural ingredients and evaluated for their organoleptic characteristics, rheological properties, spreadability, and pH levels. Furthermore, an accelerated stability assessment, freeze-thaw stability evaluation, and centrifugation analysis were conducted. Additionally, 2,2-diphenyl-1-picrylhydrazyl (DPPH) and ABTS radical scavenging assays were performed to assess their antioxidant capabilities. The creams were uniform and exhibited a pale yellowish-brown color, without any phase separation. The creams' optimum pH made them suitable for topical use. After undergoing several stability tests, the creams were found to be stable and to possess antioxidant capacity. The cream formulation was found to be skin-friendly and stable [54].

### 3.2.13. *Curcuma longa*

Curcuminoids, which are derived from *Curcuma longa*, have anti-inflammatory, anti-aging, anti-wrinkle, moisturizing, and antioxidant properties. Absolute ethanol and 85% ethanol were the two solvents used in the Soxhlet extraction of *C. longa*. The study examined all the data on anti-aging effects and nanoemulsions that were prepared and characterized. Curcumin is the most potent and unstable bioactive component of the turmeric plant. Curcumin was encapsulated in nanoemulsion droplets of medium-chain triglyceride oil produced by ultrasonication. Whey protein and Tween 80 were used as emulsifiers. Curcumin has been used in many types of research as an antioxidant. Curcumin can inhibit reactive oxygen species. Curcumin, the best-known plant-derived molecule, is a low-molecular-weight, lipophilic, yellow natural polyphenolic substance isolated from the rhizome of turmeric. People have widely used curcumin to treat aging-related disorders due to its various positive effects. It has shown a wide range of biological and pharmacological effects on drug delivery. *Curcuma longa* is the source of this natural dietary polyphenol, which possesses anti-

aging, anti-inflammatory, and antioxidant qualities. The study found that the extract of *Curcuma longa*, which has antioxidant, anti-inflammatory, and protective benefits, can enhance skin elasticity, help recover from skin deformities, improve firmness, and reduce fatigue, making it a good choice for cosmetic products aimed at reducing facial wrinkles [84].

### 3.2.14. *Ginkgo biloba* L.

The active constituents of *Ginkgo biloba* L. comprise kynurenic acid, gallic acid, protocatechuic acid, p-hydroxybenzoic acid, and ginkgolic acid. OxS is thought to be a major cause of skin aging. Wrinkles and a lifeless, dry appearance are signs of aging skin, and they are linked to the deterioration of collagen and insufficient desquamation, respectively. The findings showed that GLE pretreatment reduced MMP-1 expression and H<sub>2</sub>O<sub>2</sub>-induced cytotoxicity, which are factors in wrinkle formation. *Ginkgo biloba* leaf extract (GLE), an aqueous ethanol extract of *Ginkgo biloba* leaves, was investigated for its effects on the treatment and prevention of skin aging. The filtered extract's emulsion-based cream formulation remained stable. It was easy to apply topically. It was water-washable and stable. In an in vitro test, it was also fully absorbed via the skin. Additionally, it has been shown not to irritate the skin. It was biocompatible, uniform, and close to the skin's optimal pH for in vivo application. Additionally, there were no negative interactions, injuries, or unusual skin findings during or after the use of the prepared therapy [57]. According to the findings, GLE may have anti-aging effects on the skin by promoting desquamation by increasing the expression of kallikrein-related peptidase 7 (KLK-7), preventing wrinkles by decreasing MMP-1 expression, and shielding keratinocytes from excessive OxS by boosting the antioxidant response. GLE enhanced the key antioxidant systems, cellular glutathione levels, and HO-1 protein expression, which appeared to be triggered by the Nrf2 pathway [85].

### 3.2.15. *Clausena harmandiana*

OxS has been recognized to be harmful to human health. The existence of these disorders may arise from an imbalance between free radicals and antioxidants in the body, potentially leading to harm to the body's cells, proteins, and DNA. This kind of situation may result in several health issues, including aging. The leaves of *Clausena harmandiana* contain essential oil, predominantly composed of trans-anethole, which has significant antioxidant properties and inhibits biological processes associated with anti-wrinkle effects. As a result, the anti-collagenase and anti-elastase activities were examined and compared to a standard of oleanolic acid. The SFEQ was formulated into a microemulsion utilizing Tween 80 as a surfactant and ethanol as a co-surfactant in a 1:1 ratio. SFEQ had the most potent inhibitory effects on collagenase (IC<sub>50</sub>, 19.06±0.06 µg/mL), comparable to those of oleanolic acid (IC<sub>50</sub>, 16.75±0.14 µg/ml), followed by elastase (IC<sub>50</sub>, 121.47±2.80 µg/mL). Microemulsion formulations containing different quantities of essential oil, specifically 1% and 5% w/w, were developed and evaluated for their enzyme-inhibitory activities. The results indicated that the 5% Song Fa microemulsion inhibited collagenase and elastase (35.78% and 99.35%, respectively) more efficiently than the 1% Song Fa microemulsion (34.22% and 92.67%, respectively) [50].

This knowledge will enhance the development of essential oil-based products and optimize the use of medicinal plants in the cosmetic sector [86].

### 3.2.16. *Silybum Marianum* L.

*Silybum Marianum* L. has been shown to inhibit UVA-induced OxS; it may help treat UVA-induced skin damage. It used two superior in vitro models to assess how the recently patented anti-acne fruit extract from *Silybum Marianum* affected the synthesis and control of sebum components [87]. Human sebaceous gland organ culture (HSGOC) and sebocytes grown in a lipogenic environment using human induced pluripotent stem cells (ShiPS) were used. Fluorescence and other sebum components at the mRNA and protein levels were used to quantify lipids. *Silybum Marianum* fruit extract, in HSGOC, reduced sebum levels by 25% in the first model of sebaceous gland survival, matching the reference chemical isotretinoin by the same amount. The second model reduced lipid accumulation by decreasing the expression (at both mRNA and protein levels) of proteins involved in lipid storage and breakdown, using ShiPS *Silybum Marianum* fruit extract. Therefore, in this model, the extract effectively reduced fat accumulation by 90%. Fruit extract from *Silybum Marianum* inhibits the accumulation of fat in two seborrhea models via regulating lipid metabolism. This suggests that *Silybum Marianum* fruit extract is a promising option for controlling hyperseborrhea and adds to the results shown in patients with acne [60]. *Silybum Marianum* seed oil is generally used as an antioxidant for restoring and protecting the skin from damage that may result in wrinkles and low elasticity. *Silybum Marianum* contains both anti-wrinkle properties, allowing it to be added to cosmetic formulations [88].

### 3.2.17. *Acmella oleracea* (L.)

Spilanthol, the primary constituent of *Acmella oleracea* (L.), a member of the Asteraceae family, has been studied for the frequency of muscle contractions and the recovery of contractile activity following the inhibition of muscle contractions using a nerve-muscle coculture model. This substance inhibits subcutaneous muscles from contracting by acting similarly to Botox. In Franz-diffusion cells utilizing human skin, it has been shown that spilanthol crosses the epidermal barrier and reaches the dermis and even deeper tissues, making it possible to eliminate wrinkles in facial expressions by topical treatment. Spilanthol's ability to reduce or prevent the contraction of subcutaneous facial muscles, thereby aiding in the smoothing and minimization of expression-related wrinkles. Extracts of *A. oleracea* are widely used in anti-aging and wrinkle-preventing skincare products, with cosmetics containing spilanthol referred to as natural herbal Botox due to this characteristic [89]. Owing to its extensive range of effects, including anti-inflammatory, antioxidant, analgesic, antifungal, and bacteriostatic characteristics, it is considered a significant bioactive natural substance. Furthermore, spilanthol, as its principal bioactive constituent, impedes facial muscle contractions, rendering it a desirable element in anti-wrinkle and anti-aging cosmetics [63]. Savic et al. (2021) demonstrated in vivo a positive effect on the appearance of periorbital and perioral expression lines and wrinkles, indicating a significant enhancement in all evaluated skin wrinkle parameters, along with overall satisfactory skin tolerability and a preliminary

safety profile of the serum sample. The formulated *A. oleracea* extract-loaded natural serum, stabilized with an innovative glycolipid emulsifier, demonstrated commendable rheological and stability characteristics, effective general skin performance, and confirmed anti-wrinkle effects, positioning it as a promising topical anti-wrinkle product.

### 3.2.18. *Citrus reticulata* Blanco

Citrus species are among the most widely cultivated fruit crops globally, valued for their economic and nutritional significance. Citrus fruits, akin to other fruits and vegetables, are rich in antioxidant compounds, including polyphenols and ascorbic acid, which protect the human body against the detrimental effects of free radicals. Flavonoids are significant polyphenolic chemicals present in several components of citrus fruits, including the skin, peel, seeds, pulp membrane, and juice. Studies have demonstrated that citrus flavonoids possess health benefits, including antioxidant, anti-inflammatory, anti-aging, and anti-wrinkle characteristics [90]. The in vitro collagenase and elastase enzyme inhibitory activities of *Citrus reticulata* Blanco extract were investigated, and it showed significant anti-collagenase and anti-elastase abilities, demonstrating its potential for anti-wrinkle effects [64]. The findings indicated that *Citrus reticulata* Blanco peel cream helps reduce wrinkles [91]. Apraj et al. (2016) demonstrated that *Citrus reticulata* Blanco has the potential to inhibit the enzymes that are responsible for causing wrinkles. Due to its potential antioxidant and anti-enzymatic properties, it can serve as an effective anti-wrinkle ingredient in anti-aging skincare products [92].

### 3.2.19. *Solanum lycopersicum* Mill.

*Solanum lycopersicum* Mill. belongs to the Solanaceae family, and its main bioactive is lycopene. Due to their antioxidant properties, tomatoes can help stop free radicals from damaging skin cells. The tomato contains antioxidants such as lycopene, polyphenols, and vitamin C, which can reduce the production of free radicals like ROS and prevent collagen degradation that leads to wrinkles. Juice from tomatoes can be utilized as an alternative to traditional skincare techniques [65]. The treatment group administered the sample formulation demonstrated a 35.63% enhancement in stratum corneum hydration and a 29.39% decrease in transepidermal water loss [93].

### 3.2.20. *Veronica officinalis*

*Veronica officinalis* is a member of the Plantaginaceae family, with verbascoside as its primary phytoconstituent. The speedwell extract showed significant anti-wrinkle activity in vivo. This result may be attributed to the considerable radical scavenging activity of the speedwell extract, which neutralized free radicals in the skin, thus shielding collagen from destruction. The phytochemicals in the extract may interact with specific enzymes and mediators within the signal transduction pathway, thereby initiating anti-wrinkle benefits for the skin. *Veronica officinalis* extract serves as an effective anti-wrinkle agent in human skin.

### 3.2.21. *Anacardium occidentale* L.

Extracts of cashew leaves obtained using ethanol demonstrated significant antioxidant properties and exhibited the greatest suppression of key enzymes associated with skin aging, including collagenase. This suggests the possibility of developing cosmetic treatments targeting anti-aging,

wrinkle reduction (via collagenase inhibition), skin brightening, and antioxidant properties. The long-term stability and physical characteristics of a face cream with cashew leaf extracts were examined. Results revealed that the cream maintained satisfactory stability and physical properties under various storage conditions. Another study on *Anacardium occidentale* L. identified quercetin, chlorogenic acid, and rutin. The cashew extract, rich in flavonoids such as rutin, may contribute to its healing and antioxidant properties. The extract exhibited no cytotoxic effects on keratinocytes in vitro, confirming its safety for skin application. It was added to a topical oil-in-water emulsion, demonstrating potential for treating premature skin aging due to its antioxidant and healing characteristics.

### 3.2.22. *Isatis indigotica*

The extract's primary constituent was identified as 3,4,5-trimethoxycinnamic acid using liquid chromatography coupled with mass spectrometry. Molecular docking described the binding mechanism of 3,4,5-trimethoxycinnamic acid with matrix metalloproteinase-1 and -3, resulting in binding energies of -5.20 and -4.89 kcal/mol, respectively. The *I. indigotica* leaf extract inhibits wrinkle formation and may serve as a potential anti-wrinkle agent. This study confirmed the anti-wrinkle effectiveness of *I. indigotica* leaf extract. The study demonstrated DPPH and ABTS radical scavenging activities, along with inhibitory effects on nitrite formation and the expression of MMP-1 and MMP-3. The extract of *I. indigotica* leaves has been validated as an anti-wrinkle agent in a clinical trial for the first time. Consequently, *I. indigotica* leaf extract could be incorporated into commercial products to reduce wrinkle formation and enhance skin aging [2].

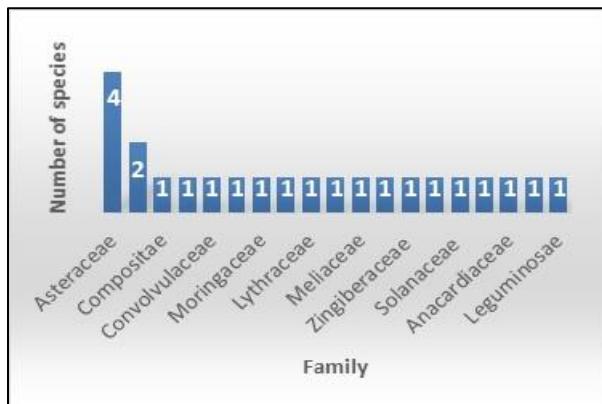
### 3.2.23. *Glycyrrhiza glabra*

*Glycyrrhiza glabra* methanolic extracts demonstrated strong antioxidant properties and the ability to inhibit enzymes that break down collagen, elastin, and hyaluronic acid, suggesting they could be a promising option for effective anti-aging products. The *Glycyrrhiza glabra* methanolic extract contained numerous phenolic compounds and was most effective in combating oxidation and inhibiting specific enzymes, whereas the water extract was less effective in these tasks. These results suggest *Glycyrrhiza glabra* could be incorporated into cosmetic formulations due to its protective effects against various enzymes, which are particularly beneficial for skin aging, especially photoaging [70]. Cerulli et al. (2022) noted that extracts from *G. glabra* and natural compounds found in licorice, particularly flavonoids, can help reduce skin aging and protect against sun damage. Glabridin, found in a commercial formulation, is claimed to have a whitening effect 1,000 times stronger than vitamin C, earning it the title of "whitening gold" and making it a popular ingredient in internationally standardized cosmetics. The antioxidant activity of functional ingredients in cosmetic products is essential, as these ingredients may assume a more significant role in these formulations. It also safeguards against oxidative damage to skin macromolecules induced by free radicals and ultraviolet light. The antioxidant activity of *G. glabra* contributes to its cosmetic uses and is generally associated with other benefits, such as photoprotection. The observed antioxidant activity attributed to flavonoids, isoflavones, and

methylated isoflavones is likely due to their phenolic content. A specific paper reviewed the antioxidant potential and biological properties of glabridin. Licochalcones B and D showed a strong ability to neutralize harmful substances in the DPPH test and could also prevent the breakdown of fats in cells. These phenolic chemicals efficiently protect biological systems from oxidative stress, minimizing skin aging damage.

#### 4. Discussion

Natural products (NPs) remain the primary source of pharmacologically active compounds for drug discovery. Historically, NPs have gained considerable attention for their advantageous effects on skin health. The use of skin care products containing phytoconstituents, such as alkaloids, phenolic acids, vitamins, flavonoids, and essential oils, has proven effective in mitigating UV radiation-induced damage, potentially managing wrinkles and minimizing harm from ultraviolet solar radiation and oxidative stress (OxS). In recent years, numerous natural molecules have garnered considerable interest due to their protective activity against UV radiation [94]. There is a significant demand for novel cosmeceutical compounds derived from plants in the personal care market, driven by increased consumer awareness of healthy products that incorporate natural components. Progress in our understanding of skin physiology and aging has led to the discovery of novel biochemical targets for skin health, which, when chemically modified, can aid in restoring and/or preserving its healthy condition. Plants are the primary source of these phytochemicals, which can rejuvenate and enhance skin health and attractiveness. The industry has utilized a multitude of plants to develop innovative cosmeceutical formulations aimed at specific goals, including allergy treatment, sun protection, anti-aging, anti-wrinkling, and antioxidant effects [95]. Medicinal plants have long been utilized as active ingredients in cosmetics and therapeutics, serving as both beautifying agents and remedies for dermatological issues, including eczema, hyperpigmentation, and photoaging. These resources present a largely untapped potential for developing active ingredients in cosmetic formulations. Around 23 plant sources used in this review, belonging to the 19 plant families: Ebenaceae, Convolvulaceae, Compositae, Lamiaceae, Moringaceae, Asteraceae, Apiaceae, Lythraceae, Poaceae, Meliaceae, Clusiaceae, Zingiberaceae, Ginkgoaceae, Rutaceae, Solanaceae, Plantaginaceae, Anacardiaceae, Cruciferae, and Leguminosae, as shown in Fig. 6., are reviewed scientifically for their cosmeceutical claims.



**Fig. 6.** Plant families with the highest number of species used to treat wrinkles.

Srisuksomwong et al. (2023) demonstrated that plant extracts are extensively utilized in cosmetics for various applications, including whitening, moisturizing, UV protection, anti-wrinkle treatments, preservatives, antioxidants, and thickeners. Anti-wrinkle solutions derived from natural plant extracts are gaining popularity as efficient, safe, and non-toxic alternatives to traditional cosmetic products. Antioxidants are widely used in anti-wrinkle cosmetics for their capacity to scavenge free radicals, thereby mitigating or preventing skin oxidative stress and managing wrinkles. This study identified various phytoconstituents, including uronic acid, galacturonic acid, ferulic acid, gallic acid, 1,2,4-butanetriol, quercetin, rutin,  $\alpha$ -pinene, sabinene, geraniol, linalool, kaempferol, moringinine, niazzine A, niazirin, alpha-tocopherol, catechin, epicatechin, ellagitannin, gallotannin,  $\gamma$ -oryzanol, phytic acid, garcinone C, garcinone D, curcumin, gamma-mangostin, alpha-mangostin, and shikimic acid, 6-hydroxy kynurenic acid, protocatechuic acid, p-hydroxy benzoic acid, ginkgolic acid, trans-anethole, silymarin, silybin A & B, isosilybin A & B, silychristin, isosilychristin, silydiamin, spilanthol, vitamin C, lycopene, verbascoside, chlorogenic acid, and 3,4,5-trimethoxycinnamic acid. All these phytoconstituents possess the capability to mitigate wrinkles. They may also block UV light and other elements that contribute to the formation of wrinkles. An overview of how direct sunlight produces reactive oxygen species (ROS) can enhance the capacity of activator protein-1 (AP-1) to upregulate protein expression. The buildup of unmetabolized fibers in the skin, resulting from UV-induced enzymatic degradation of elastin and collagen, contributes to the intricate process of skin wrinkling. Pollutants, ultraviolet light, smoking, and xenobiotics produce exogenous reactive oxygen species in the human body. Reactive oxygen species compromise antioxidant defense mechanisms, leading to considerable oxidative stress and contributing to the development of wrinkles, inflammation, cell proliferation, and other adverse effects. Moreover, these reactive oxygen species (ROS) result in the excessive synthesis of elastases, a decrease and deterioration of collagen, and the accumulation of glycosaminoglycans. These data suggest that antioxidants play a crucial role in neutralizing reactive oxygen species for wrinkle control. As a result, cosmeceuticals are rapidly emerging as a burgeoning market segment, driven by the increasing demand for individuals to maintain healthy skin without the use of chemical treatments. Novel and emerging trends in natural beauty products are prompting academics to develop innovative solutions. Persistence Market Research and Grand View Research indicate that the demand for natural and organic personal care products worldwide is rising and is projected to continue growing. Consequently, there is a growing global demand for plant extracts used in anti-wrinkle and other cosmeceutical applications, due to their low incidence of adverse effects. Scientific research has demonstrated that phytoconstituents have a prominent role in the beauty industry, making them an advantageous option for wrinkle treatment. This review examines the application of natural bioactive compounds in anti-wrinkle treatments within dermatology and cosmeceuticals. Fig. 7 and Fig. 8. show the plant parts used for the treatment of wrinkles, and the percentage of formulation used for the treatment of wrinkles.

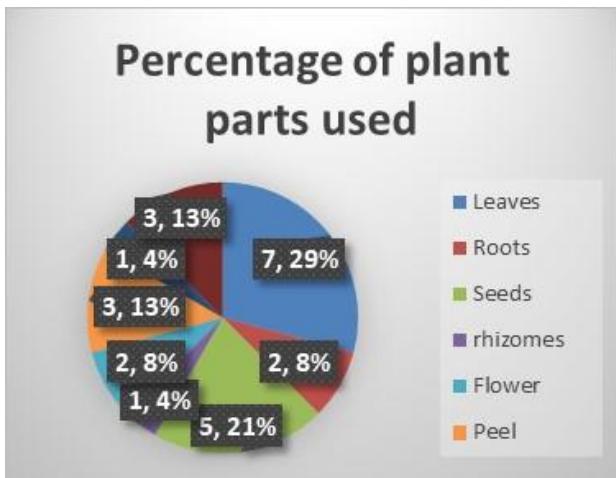


Fig. 7. Plant parts are used for the treatment of wrinkles.

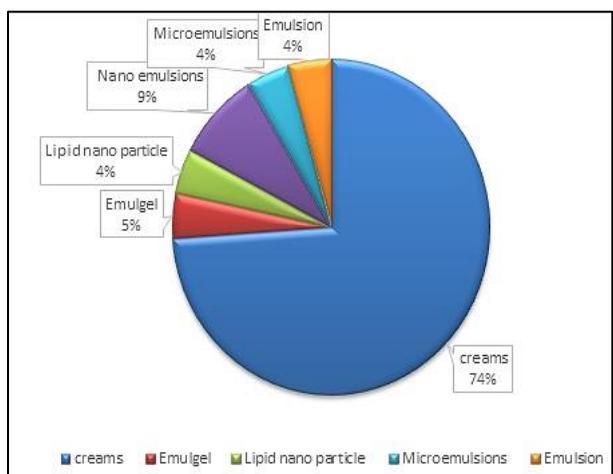


Fig. 8. Percentage of formulation used for the treatment of wrinkles.

#### 4.1. The Role of Phytoconstituents

In this review, flavonoids, phenols, and essential oils were found useful for managing wrinkles.

##### 4.1.1. Flavonoids

Formulations enriched with phytoconstituents are preferable due to their biodegradability and low toxicity. Phenolic chemicals, flavonoids, essential oils, antioxidants, and various other phytoconstituents are among the numerous plant metabolites [96]. These chemicals seem to be beneficial in mitigating damage induced by UV radiation. Flavonoids found in nature help maintain skin suppleness by significantly inhibiting the up-regulation of MMPs. Additionally, various studies have demonstrated that flavonoids exhibit strong anti-elastase activity. Therefore, flavonoids' anti-elastase action may be responsible for the enhanced skin elasticity reported in multiple investigations. The improved skin elasticity may account for the elevated smoothness index. Fine and coarse lines diminish as elasticity and moisture increase, resulting in a smoother skin that becomes firmer, tighter, and less loose.

##### 4.1.2. Phenol

The phenolic compounds that enhance the skin's moisture index may explain this decrease. Skin scaliness decreases in direct correlation with elevated moisture levels. The formulation led to a reduction in the skin wrinkle index. The skin scaliness index is directly correlated with

skin dryness. The scaliness index of the skin decreases as the moisture index increases, and conversely, they exhibit an inverse relationship. The presence of phenolic chemicals in formulations that improved the skin moisture index may account for this reduction. Scaliness of the skin diminishes with elevated moisture levels [28].

##### 4.1.3. Antioxidant

Antioxidants prevent the oxidation of harmful free radicals generated by physiological and environmental stress, which contributes to aging and the development of wrinkles. [97]. This study investigates the use of formulations and herbal extracts in the creation of cosmetic products that counteract external signs of skin aging, including wrinkles. The article highlights the harmful effects of prolonged sun exposure and the increasing desire for natural anti-wrinkle solutions. Herbal extracts from medicinal plants are selected for their therapeutic efficacy and fewer adverse effects relative to manufactured drugs. These extracts function as vehicles for plant bioactives. The medicinal herbs identified in this analysis exhibit anti-wrinkle potential and antioxidant properties, aiding in wrinkle prevention and restoring skin flexibility.

##### 4.1.4. Essential oil

Essential oils are essential in the creation of cosmetics due to their numerous uses and the complex composition of their active ingredients. Essential oils offer a variety of dermatocosmetic benefits when added to skincare products, including anti-aging, anti-wrinkle, skin-lightening, and sun protection advantages [98]. This review finds essential oils effective for anti-wrinkle applications. Bioactive substances derived from plants have the potential to modulate the age-related degradation of cells. Nowadays, people seek solutions to maintain a youthful appearance with smooth skin and its benefits. Photoprotection is a fundamental mechanism for combating photoaging, which has the potential to reduce wrinkles.

Additionally, herbal cosmetics can serve as a therapeutic approach. In this review, we have selected 23 anti-wrinkle plants that contain various phytochemicals, including flavonoids, essential oils, phenols, polyphenols, carotenoids, alkaloids, vitamins, and antioxidants, which are associated with anti-wrinkle activity. In the selected formulations, the majority found was cream; only two formulations contained nanoemulsion, while another was found in a single number. Based on these formulation findings, it can be concluded that researchers can move toward nanoemulsions because they improve the distribution and absorption of active substances due to their small particle size. This may enhance their ability to penetrate the skin's deeper layers and provide more noticeable effects. By utilizing nanoemulsions, the stability of the active ingredients can be improved, protecting them from environmental factors that could cause deterioration. This may help maintain the product's efficacy and shelf life. Creams can leave a residue on the skin and are often thicker. Although they may seem greasy or heavy, they can be hydrating, especially for people with oily skin. The skin feels smooth and non-greasy after using nanoemulsions because they are typically lighter and easier to absorb. This can be especially helpful for those with oily skin or combination skin types. Both creams

and nanoemulsions offer benefits. Traditional creams are generally easier to use and sometimes more effective, whereas nanoemulsions offer better penetration, stability, and potential for enhanced efficacy. We have reviewed publications from the past 15 years and carefully compiled the most relevant facts. Multiple databases, specifically PubMed, Google Scholar, Web of Science, and Scopus, were utilized as sources of literature [99]. Natural chemicals have been utilized in skincare for centuries. An effort is underway to discover novel natural bioactives that enhance skin health and protect the skin from detrimental elements, such as UV radiation and free radicals. Conversely, cosmetics are products utilized for skin care and cleansing, enhancing aesthetic appeal, and promoting well-being without impacting biological organs, components, or functions. Plant-derived bioactive compounds are in great demand as active ingredients in the cosmeceuticals sector due to their therapeutic properties, including moisturizing, rejuvenating, anti-wrinkle effects, UV protection, and the prevention of skin disorders. Natural bioactive plant chemicals are favored for their eco-friendliness and compatibility with diverse skin types, devoid of the synthetic chemical components that frequently induce skin irritation [38].

#### **4.2. Future Challenges and Prospects in Plant Extracts and Phytoconstituents for Treating Wrinkles**

There are numerous prospects in the investigation of plant extracts and phytoconstituents for treating wrinkles, but several obstacles must be overcome to fully utilize their potential in skincare products. Researchers, formulators, and consumers alike must understand these opportunities and challenges as the market for natural and effective skincare products expands.

##### **4.2.1. Stability and Formulation Challenges**

One of the primary challenges in developing effective plant-based skincare formulations is ensuring the stability of active ingredients, as plant extracts are sensitive to environmental factors like light, heat, and oxygen, which can lead to degradation and reduced efficacy over time. Formulating stable emulsions, creams, and lotions with plant-based ingredients is particularly difficult; formulators must carefully choose emulsifiers and stabilizers to maintain product integrity while incorporating bioactive compounds. Additionally, batch variability poses a challenge, as the consistency of plant-based ingredients can fluctuate due to factors such as growing conditions, harvest time, and extraction methods, which complicates formulation processes and potentially results in inconsistent product performance.

##### **4.2.2. Regulatory Compliance**

Navigating regulatory frameworks is essential for the successful commercialization of plant-based skincare products. Different countries have varying regulations concerning the use of natural ingredients in cosmetics, requiring manufacturers to ensure that all components comply with local regulations. This often involves extensive research and documentation to demonstrate the safety and efficacy of the products. Additionally, there is a growing demand for sustainably sourced plant materials, which presents another challenge, as manufacturers must ensure that their sourcing practices align with ethical standards while maintaining product

quality, adding complexity to the formulation and production processes.

##### **4.2.3. Consumer Awareness and Education**

As consumers become more informed about skincare products, there is an increasing expectation for transparency regarding ingredient sourcing, formulation processes, and product efficacy. Manufacturers must invest in educating consumers about the benefits of plant extracts in treating skin conditions, such as wrinkles, by providing clear communication on how these ingredients work and their advantages compared to synthetic alternatives. Additionally, addressing misconceptions is crucial, as many people believe that natural products are inherently safer or more effective than synthetic options. It is essential to clarify that "natural" does not always equate to safety or effectiveness without proper formulation, underscoring the importance of informed consumer choices in the skincare market.

##### **4.2.4. Advancements in Extraction Techniques**

Innovative extraction methods have significantly enhanced the bioavailability and stability of phytoconstituents used in skincare formulations. The adoption of green extraction techniques, such as natural deep eutectic solvents, has improved the efficiency of extracting bioactive compounds while minimizing environmental impact. These environmentally friendly methods enable the recovery of valuable phytochemicals without the use of harmful solvents. Additionally, advancements in nanotechnology offer promising solutions for enhancing delivery systems in plant-based formulations. By enhancing the solubility, stability, and controlled release profiles of active ingredients, these technologies can lead to more effective skincare products that fully harness the potential of plant extracts.

##### **4.2.5. Market Trends and Future Prospects**

The prospects for plant-based skincare formulations are promising due to several emerging trends. There is a growing demand for natural products as consumers increasingly seek sustainable and ethical options, driving significant market growth for plant-based skincare. Companies are investing heavily in research and development to create innovative formulations that meet the evolving demands of consumers. Additionally, the trend toward personalized skincare solutions presents opportunities to integrate plant extracts tailored to individual skin types and concerns, potentially enhancing treatment efficacy for conditions like wrinkles. Furthermore, the incorporation of technology in skincare, such as apps that analyze skin conditions, could assist consumers in selecting appropriate products containing specific plant extracts based on their unique needs.

## **5. Conclusions**

This thorough review highlights the increasing importance of phytoconstituents in contemporary skincare, particularly for the prevention and treatment of wrinkles. There is a noticeable shift toward botanical ingredients, which are known for their safety, effectiveness, and environmental friendliness, as a result of growing awareness of the negative effects of synthetic chemicals. The phytochemicals extracted from various

parts of medicinal plants exhibit strong antioxidant, anti-inflammatory, photoprotective, and enzyme-inhibitory properties, all of which support their potential in preventing aging. These characteristics enable them to combat oxidative stress, inhibit the enzymes collagenase and elastase, and stimulate the production of collagen and elastin, all of which are crucial for maintaining skin suppleness and preventing wrinkles.

Traditional medicine has employed botanical extracts for centuries, and recent research confirms their efficacy in cosmeceutical formulations. They are helpful in dermatological treatments as well as cosmetic applications due to their ability to protect skin cells from environmental stressors and UV-induced damage. A strong argument is also made for the wider use of phytoconstituents in the skincare sector due to their multipurpose nature, which enables them to function as antioxidants, UV protectants, moisturizers, and structural skin enhancers simultaneously.

In the future, this research will have consequences that go beyond cosmetic applications. The development of targeted, effective, and sustainable phytoformulations holds enormous potential for the future, driven by advancements in green chemistry, nanotechnology, and biotechnology. It is anticipated that plant-based actives will play a central role in emerging trends, such as customized skincare, microbiome-friendly products, and biosensor-driven delivery systems. There is a significant opportunity for future research to discover new agents with enhanced anti-wrinkle and regenerative properties, as many bioactive compounds from plants remain unexplored.

Future studies must concentrate on standardizing extraction techniques, refining formulations, and conducting carefully planned clinical trials to determine the efficacy and safety profiles of phytoconstituents, in order to fully utilize them. Global quality standards and regulatory frameworks will also be essential in guaranteeing reliable performance and customer confidence. Phytoconstituents represent a potential frontier for innovative, scientifically validated anti-aging therapies in the global cosmetics industry. They provide a more secure and organic alternative to synthetic agents.

**Author Contributions:** Conceptualization, A.K. and M.P.; methodology, A.K.; validation, M.P., V.R., and A.K.; investigation, A.K.; resources, M.P.; data curation, V.R.; writing-original draft preparation, A.K.; writing-review and editing, A.K., M.P.; visualization, M.P.; supervision, V.R. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research received no external funding.

**Acknowledgments:** The author acknowledges the Chancellor, Vice-Chancellor of Teerthanker Mahaveer University, and Principal of Teerthanker Mahaveer College of Pharmacy, Moradabad, for providing the necessary facilities and constant support while preparing the manuscript.

**Conflicts of Interest:** The authors declare no conflict of interest.

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