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Review

Traditional Herbs in Anatolian Medicine for Rosacea: A Basis for Non-Steroidal Magistral Therapy

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Abstract

Rosacea is a chronic inflammatory disorder with a prevalence reported between less than 1% and 22% across populations, increasing annually. In the context of rosacea management, numerous aspects of the condition's pathophysiology remain insufficiently understood. Despite the availability of various topical and oral treatments and laser therapies for rosacea, their limitations, common adverse effects, and high costs frequently lead to premature discontinuation, driving greater interest in plant-based formulations among both clinicians and patients. Consequently, herbal products containing natural ingredients are increasingly preferred over synthetic alternatives, owing to their multiple benefits and lower frequency and severity of side effects. This review emphasizes that a range of herbal extracts and oils, traditionally used in Anatolian medicine which is supported by literature mainly for their anti-inflammatory, antioxidant, antimicrobial, and anti-erythematous effects, possess significant potential in managing rosacea. Drawing on recent preclinical and clinical studies, Our study outlines the mechanisms by which various phytochemicals alleviate the clinical symptoms of rosacea, thereby enhancing understanding of the therapeutic potential of plant-based products and guiding future researches.

Keywords: rosacea; Anatolian medicine; herbal extracts; essential oils; anti-inflammatory; antioxidant; macerated oils; anti-erythematous

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1. Introduction

Rosacea is a long-term inflammatory disease that mostly affects the eyes and the centrofacial area, which includes the cheeks, chin, nose, and forehead [1]. The prevalence of rosacea is higher in women than in men. Moreover, rosacea is more commonly observed among individuals with fair complexions, particularly those of Celtic and Northern European ancestry. Episodes of exacerbation and remission are hallmarks of the illness, which is typically first seen in individuals between the ages of 30–50. According to literature, the prevalence of rosacea varies from less than 1% to 22% in different populations [1,2].

The National Rosacea Society Expert Committee first used a subtypes approach to classify rosacea, with four main subtypes: phymatous, ocular, papulopustular, and erythematotelangiectatic. Facial erythema, frequently with telangiectasias present, is a characteristic of erythematotelangiectatic rosacea. Facial erythema and varying numbers of erythematous papules and pustules are the initial signs of papulopustular rosacea. Phymatous rosacea is characterized by skin thickness and sebaceous gland hyperplasia, frequently in the nasal area (rhinophyma). Chalazion, conjunctivitis, and blepharitis are common symptoms of ocular rosacea. Other dermatoses can also coexist with rosacea [1–3]. Nevertheless, rosacea is a complicated illness that can present with numerous subtypes, progress between subtypes, and coexist with other dermatoses. Patients may not easily fit into a single subtype. Rigid subtype classification of diagnoses can hinder severity evaluation and comprehensive coverage of clinical presentation and negatively impact patient outcomes. As a result, the Global Rosacea Consensus Panel recommends a more patient-focused phenotypic approach, which is currently the most often utilized method in clinical practice. In the phenotyping approach, the phymatous changes are taken into consideration for the cutaneous rosacea diagnosis. Major features include papules/pustules, flushing/blushing, and telangiectasis, while minor features include stinging, burning, dryness, and edema. The severity of the rosacea features is also an important parameter for the phenotyping method [2,3].

Although the exact pathophysiology of rosacea is unknown, the disease is related to immunological dysregulation, neurovascular dysregulation, microorganisms, hereditary factors, and a variety of environmental factors [4]. One significant factor of the pathophysiology of rosacea is immunological dysregulation. Cytokine and antimicrobial peptide synthesis rises when the innate immune system is activated. Higher baseline levels of cathelicin and kallikrein 5 (KLK5) are observed in the lesional skin of rosacea patients [4,5]. The pathophysiology of rosacea is influenced by mast cells. Mast cells secrete LL-37, which affects mast cell function by causing chemotaxis, degranulation, and the production of proinflammatory cytokines such as MMP-9 and interleukin 6 [6]. When LL-37 was injected into mast cell null mice in an in vivo mouse model study, no inflammation was seen. Injection of LL-37 caused inflammation in mice that were reconstituted with mast cells, indicating that mast cells contribute to the inflammatory condition of rosacea [7]. Additionally, prior studies have shown the effects of *Bacillus oleronius*, *Staphylococcus epidermidis*, *Helicobacter pylori*, *Bartonella quintana*, and *Demodex* spp. on the development of rosacea. However, the exact pathophysiology of rosacea remains unclear [5]. Another well-known trigger of rosacea is UV light. Rosacea symptoms may intensify as a result of UV light exposure [4]. Transient receptor potential (TRP) cation channels, which are widely expressed on neuronal and non-neuronal cells such as keratinocytes and endothelial cells, have improved the current knowledge of the pathophysiology of rosacea. These vasoregulatory neuropeptides serve as critical mediators that generate the persistent flushing characteristic of rosacea. The TRPV1 receptor, expressed by sensory nerves and keratinocytes, is expressed at higher levels in patients with rosacea. It is stimulated by heat, ethanol, inflammation, and capsaicin, and it contributes to vasoregulation and nociception [4,5]. Various topical and oral therapies may be utilized in the treatment of rosacea. Several are FDA-approved, including metronidazole, ivermectin, azelaic acid, and oral doxycycline. Nevertheless, the majority of medications, whether FDA-approved or not, exhibit numerous adverse effects, leading patients to discontinue treatment prior to the emergence of beneficial effects on their skin. Additionally, the recovery effects of laser and light-based therapies—especially pulsed dye lasers (PDLs), neodymium yttrium–aluminum–garnet (Nd:YAG) laser, and intense pulsed light (IPL)—against erythema and telangiectasia have been shown; however, their application is constrained by substantial costs, and further investigations are necessary

to advance understanding and improve therapeutic outcomes in this field. In addition, laser and light-based therapies may result in significant adverse effects, especially when the chosen device is not appropriately tailored to the patient's specific skin characteristics. For this reason, there is currently a tendency towards formulations obtained from plants by both doctors and patients [8–10].

Natural products that are part of numerous traditional medicinal systems have been utilized to prevent and/or treat several diseases for thousands of years in different parts of the world. For instance, Ayurveda, Tibetan medicine, traditional Chinese medicine, Anatolian medicine, and the Unani (Arabic) medicine systems have been practiced for various purposes from the past to the present for the prevention and treatment of various diseases. Today, approximately one-quarter of modern pharmaceuticals continue to be sourced from plants [11,12]. Research indicates that plants collectively synthesize over 100,000 secondary metabolites, which can be classified according to their chemical composition, biosynthetic pathways, or structural characteristics. The secondary metabolites of plants, such as polyphenols (flavonoids, anthocyanins, and phenolic acids), terpenes, alkaloids, licochalcones, saponins, carotenoids, trace elements, and vitamins, are promising due to their various biological activities [12–14]. Plant-derived natural products are increasingly gaining recognition due to several advantages, including their effectiveness, a lower incidence of side effects, greater patient tolerance, cost-effectiveness, and broad acceptance stemming from their longstanding past and traditional uses by the people. Dermatological diseases have likewise been influenced by this approach, with plant-based treatments proving to be highly effective in the management of various skin disorders [15]. Medicinal plants used in the treatment of skin disorders exhibit a range of pharmacological properties, including antibacterial, antifungal, antioxidant, anti-inflammatory, and wound-healing effects [16,17]. Türkiye possesses a remarkable diversity of macro- and microclimates, along with a rich array of vegetation types, due to the convergence of three major phytogeographic regions: the Euro-Siberian, Mediterranean, and Irano-Turanian. This unique interplay of geology, geography, topography, and climate gives rise to exceptional levels of plant diversity and endemism. Anatolian medicine has likewise benefited from this rich botanical diversity, with traditional plant-based remedies being utilized in the treatment of a wide range of ailments [18,19]. Anatolian medicine refers to the traditional medicinal knowledge and healing practices that originated and developed in the region of Anatolia (Türkiye and parts of neighboring regions). This multifaceted medicinal system is shaped by the cultural and intellectual contributions of numerous civilizations that inhabited the region over millennia, including the Hittites, Greeks, Romans, Byzantines, Seljuks, and Ottomans [20–22]. Herbal therapies have been employed for centuries in the treatment of dermatological conditions across Anatolian medicine. The effectiveness of these plants has been shown by in vitro, in vivo, and clinical studies. Traditional practices and ethnobotanical knowledge preserved in herbal manuscripts can serve as a foundational resource, guiding the discovery of novel bioactive natural compounds for the treatment of various challenging dermatological conditions [17,23].

The aim of this review is to summarize the herbal extracts and oils determined based on their traditional use in rosacea. Thus, the synthesis of evidence from preclinical and clinical studies demonstrating the efficacy of herbal extracts and oils in the management of rosacea will serve as a reference for healthcare professionals and researchers investigating these agents as potential alternative or complementary therapeutic options.

2. Methodology

This review aims to address the systematic compilation of information regarding the use of traditional plants in the treatment of rosacea. During the research, plants used in

traditional Anatolian medicine were particularly investigated. Taking into account the historical uses of plants, relevant clinical, in vitro, and in vivo studies were reviewed, and plant extracts and oils with demonstrated potential were identified. The review encompasses an overview of the pathophysiology of rosacea, alongside a detailed examination of key herbal extracts and oils with demonstrated therapeutic potential.

A comprehensive search was conducted across scientific databases, including Web of Science, Springer, MDPI, PubMed, and Google Scholar, from September 2025 until October 2025. Articles were searched in the databases mentioned using the following keywords with the Boolean operators "or" and "and": rosacea, plants, phytotherapy, herbal therapy, traditional medicine, skin diseases, and Anatolian medicine. Studies were included if they were directly or indirectly relevant to rosacea or rosacea-related inflammatory skin conditions, with a focus on herbal extracts and oils derived from plants used in traditional Anatolian medicine. Clinical, in vitro, and in vivo studies were considered. Articles were excluded if they were not related to dermatological applications or did not address rosacea or its key pathophysiological features. The figure is original and was designed using Microsoft PowerPoint (version 2010).

3. The Plants Effective in Rosacea Therapy

The plants that are effective in the management of rosacea, along with their active compounds and activities for rosacea, are summarized in Table 1. Additionally, the mechanisms of action of Anatolian medicinal plants used in the management of rosacea are shown in Figure 1. Although some of these plants have not been specifically examined in the context of rosacea, they have demonstrated efficacy in alleviating symptoms commonly associated with the condition—particularly anti-inflammatory, antioxidant, antimicrobial, and vasoprotective effects. Consequently, they warrant further investigation for their potential to target the two principal characteristics of rosacea: erythema and papules.

Table 1. Plants used in the management of rosacea.

Plant	Active Compounds	Activity/Mechanism	Reference
Glycyrrhiza glabra L. Extract	Saponins (glycyrrhizic acid–glycyrrhizin, glycyrrhetinic acid), Chalcones (isoliquiritigenin, licochalcone A, isoliquiritin), Flavanones (liquiritigenin, liquiritigenin apiosyl glucoside, liquiritin, licoflavone A, kaempferol, glabrin A, glabrin B, apigenin rutinoside), and Isoflavones (isoangustone A, glabridin, formononetin)	Anti-inflammatory, Antioxidant, Anti-allergenic, Anti-immune-mediated cytotoxicity, Anti-erythematous, Anti-irritant	[24–46]
Matricaria recutita L. Extract and Essential Oil	Phenolic acids (caffeic acid, chlorogenic acid, p-coumaric acid), Flavanones (apigenin, luteolin, penduletin, rutin, quercetin, and their derivatives), Terpenes (α-bisabolol, bisabolol oxide A, bisabolol oxide B, β-farnesene, chamazulene, and matricin), and Coumarins (umbelliferone, herniarin, and 7-methoxy-coumarin)	Anti-inflammatory, Antioxidant, Anti-allergenic, Analgesic, Antimicrobial, Antiangiogenic	[47–65]

Table 1. *Cont.*

Plant	Active Compounds	Activity/Mechanism	Reference
Rosa canina L. Seed Oil	Unsaturated Fatty Acids (α-linolenic, linoleic, and oleic acids), Phytosterols (β-sitosterol, campesterol, stigmasterol, Δ5 avenasterol, and Δ7 avenasterol), Tocopherols (α-, γ-, and δ-tocopherol), Carotenoids (β-carotene, lycopene, zeaxanthin, and lutein), and Polyphenolic compounds (methyl esters of p-coumaric acid, vanillic acid, and 4-hydroxybenzoic acid)	Anti-inflammatory, Antioxidant, Antimicrobial, Anti-aging	[66–84]
Hypericum perforatum L. Macerated Oil	Naphthodianthrone derivatives (hypericin and pseudohypericin), Acylated phloroglucinols (hyperforin and adhyperforin), and Flavonoids (quercetin, quercitrin, hyperoside, rutin, kaempferol, biapigenin, and amentoflavone)	Anti-inflammatory, Antioxidant, Antimicrobial	[85–97]
Calendula officinalis L. Macerated Oil	Triterpenoids, along with their esters (faradiol, taraxasterol, and lupeol; faradiol-3-palmitate and faradiol-3-myristate), Carotenoids (lutein, β-carotene, flavoxanthin, and rubixanthin), and Flavonoids (quercetin, isorhamnetin, kaempferol, and their derivatives)	Anti-inflammatory, Antioxidant, Antimicrobial	[98–112]
Rosa damascena Miller (Damask Rose) Essential Oil	Terpenes (citronellol, geraniol, nerol) and Aliphatic hydrocarbons (nonadecane, heptadecane, and heneicosane)	Anti-inflammatory, Antioxidant, Antimicrobial, Anti-aging	[113–126]
Origanum vulgare L. (Common Oregano) Essential Oil	Terpenes (carvacrol, thymol, linalool, γ-terpinene, and p-cymene)	Anti-inflammatory, Antioxidant, Antimicrobial, Anti-aging	[127–139]

Figure 1. The mechanisms of action of Anatolian medicinal plants used in the management of rosacea.

3.1. Glycyrrhiza glabra L. (Licorice) Extract

Since the earliest historical records, *Glycyrrhiza glabra* L. has been employed as a therapeutic agent in traditional medicine. The root part of *G. glabra* has been traditionally utilized in herbal medicine for the treatment of various skin conditions, including dermatitis, eczema, pruritus, and cutaneous cysts [25]. The plant has been used in Anatolian medicine for thousands of years, and today Türkiye is one of the important commercial production centers [26]. The earliest documented reference to the use of the root of licorice for treating skin lesions can be traced back to Theophrastus. Plinius, Dioscorides, and Ibn Sina also mentioned that the plant could be used on wounds and ulcers [27]. *G. glabra* is particularly abundant in saponins (glycyrrhizic acid, glycyrrhetinic acid), chalcones (isoliquiritigenin, licochalcone A, isoliquiritin), flavanones (liquiritigenin, liquiritin, licoflavone A, kaempferol), and isoflavones (isoangustone A, glabridin, formononetin), which represent the major classes of the plant's bioactive constituents [24–46]. Glycyrrhizin, also called glycyrrhizic acid, is the principal phytochemical compound; it typically comprises 5–10% of dried root, occasionally reaching up to 16% depending on the region and extraction method of *G. glabra* [40]. Additionally, *G. glabra* is officially recognized in the Japanese Pharmacopoeia, which mandates a minimum glycyrrhizic acid content of 2.0% (based on dry weight) as a criterion for quality assurance [41]. Glycyrrhizin (13.927 mg/g dry extract) was determined to be the most abundant compound of the *G. glabra* ethanolic extract by Semenescu et al. [42]. One of the most remarkable characteristics of glycyrrhizin—potentially the main contributor for the licorice extract's therapeutic efficacy—is its capacity to integrate into the lipid bilayer, thereby enhancing membrane fluidity and permeability. This ability of biomolecules and their assemblies to modulate cellular membrane properties holds substantial importance from both fundamental biological and applied biomedical perspectives. This interaction, in turn, also amplifies the bioactivity of other phytochemical constituents present in the extract or herbal products [43]. Glabridin is the most abundant isoflavone in licorice root, ranging from 0.08% to 0.35% of dry weight [44]. In studies investigating regional variation, glabridin concentrations ranging from 0.15 to 2.92 mg/g of dry weight were also reported, with these differences attributed to the geographic origin of cultivation [45]. Liquiritin (5.037 mg/g dry extract), liquiritigenin-apiosyl-glucoside (2.946 mg/g dry extract), apigenin-rutinoside (2.571 mg/g dry extract), and liquiritigenin (1.268 mg/g dry extract) were also determined to be the major compounds of the *G. glabra* ethanolic extract by Semenescu et al. [42]. The concentration of licochalcone A in *G. glabra* root generally ranges from 0.3% to 1% *w*/*w*; however, certain studies have documented levels as high as 8–10 mg per gram of dry root extract [46]. The anti-inflammatory, antioxidant, anti-allergenic, anti-immune-mediated cytotoxicity, and anti-erythematous activities of *G. glabra* have been reported in the literature. The antioxidant activity of the *G. glabra* supercritical extract was shown by Quintana et al., and the strong activity was attributed to the high content of phenolic compounds (liquiritin, liquiritigenin, glycyrrhizin, isoliquiritigenin, and glabridin) in the extract [30]. Although there are studies examining the effects of licorice root extract on the skin, the vast majority of studies were performed with the chalcones (especially licochalcone A and isoliquiritigenin), isoflavones (especially glabridin), saponins (especially glycyrrhizic acid–glycyrrhizin and glycyrrhetinic acid), and flavanones (especially licoflavone) of licorice [31–40].

In an open-label clinical study involving 62 participants, it was demonstrated that licochalcone A—a flavonoid derived from licorice root—significantly reduced erythema in rosacea patients following once-daily topical application over an eight-week period. Furthermore, when co-administered topically with the antibiotic metronidazole in a subset of 25 patients, the formulation was well tolerated. The findings support the routine use of licochalcone A-containing skincare products for individuals with rosacea and facial

erythema, contributing to improvements in both skin appearance and quality of life [31]. In another study that involved healthy individuals, it was determined that applying oil-in-water lotions containing either 0.025% or 0.05% of aqueous extract containing licochalcone A from another *Glycyrrhiza* species (*Glycyrrhiza inflata* Batalin) twice a day for three days significantly decreased the amount of erythema caused by shaving and UV exposure when compared with a vehicle control. Licochalcone A's potent inhibition of in vitro pro-inflammatory responses, including N-formyl-MET-LEU-PHE (fMLP)- or zymosan-induced oxidative burst of granulocytes, UVB-induced PGE2 release by keratinocytes, lipopolysaccharide (LPS)-induced PGE2 release by adult dermal fibroblasts, fMLP-induced LTB4 release by granulocytes, and LPS-induced IL-6/TNF-α secretion by monocyte-derived dendritic cells, was also shown in the study [32]. The therapeutic potential of a formulation combining licochalcone A and trans-4-t-butylcyclohexanol—an inhibitor of the TRPV1 cation channel—was evaluated in an open-label, international, multi-center study. TRPV1, which is expressed in the skin, mediates sensations such as pain, itching, and warmth; its activation in keratinocytes leads to increased calcium influx, ultimately resulting in cell death and disruption of the epidermal barrier. In this study, 1221 individuals with sensitive, redness-prone, and rosacea-affected skin received the combination treatment twice daily. After four weeks, a notable improvement in clinical symptoms, including redness and erythema, was observed [33]. In a study conducted by Schoelermann et al., the anti-irritant and anti-erythematous activities of a skin care regimen (consisting of a cleanser, a day care with SPF25, and a night care) containing licochalcone A from the licorice plant *G. inflata*, and 4-t-butylcyclohexanol (SymSitive®, Holzminden, Germany) were demonstrated over 8 weeks with 32 mild to moderate rosacea participants [34]. Isoliquiritigenin, a chalcone molecule, ameliorated the overall manifestation of atopic dermatitis-like symptoms, including scratching behavior incidence and skin lesion severity, and suppressed of 2,4-dinitrochlorobenzene-induced IgE and Th2 cytokine up-regulation at the blood level was shown by Yu et al. [35]. It was demonstrated by Yokota et al. that UVB-induced pigmentation and erythema in the skin of guinea pigs were effectively inhibited by topical applications of 0.5% glabridin. The anti-inflammatory effects of glabridin's (isolated from the hydrophobic (ethyl acetate–type) fraction of licorice extract) in vitro were also demonstrated by its inhibition of superoxide anion production and cyclooxygenase activities [36]. Xie et al. reported that the addition of diammonium glycyrrhizinate—a saponin and glycyrrhizin salt—to a treatment regimen of clarithromycin and isotretinoin enhanced therapeutic efficacy in rosacea patients compared to the use of clarithromycin and isotretinoin alone [37]. M. Saeedi et al. conducted a double-blind clinical trial to assess the efficacy of *G. glabra* extract, standardized to glycyrrhizinic acid (glycyrrhizin), in the management of atopic dermatitis. Topical formulations containing 1% and 2% of the extract—prepared using propylene glycol as a co-solvent and Carbopol 940 as a gelling agent—were evaluated against a base gel. Over a two-week treatment period, the 2% licorice gel significantly reduced erythema, edema, and pruritus, demonstrating notable therapeutic potential for atopic skin. Given that rosacea also presents with sensitive skin, inflammation, erythema, and pruritus, it may be inferred that *G. glabra* extract holds promise as an effective topical agent for rosacea management as well [25]. The inhibition of histamine synthesis by glycyrrhetinic acid in mast cells cocultured with Swiss 3T3 fibroblasts was shown by Lee et al. [38]. Frattaruolo et al. conducted a comprehensive study demonstrating that *G. glabra* leaf ethanol 96% extract—obtained via both maceration and ultrasound-assisted extraction—exhibits strong antioxidant and anti-inflammatory properties. The extract was shown to suppress lipopolysaccharide-induced expression of pro-inflammatory cytokines, including TNF-α, IL-1, and IL-6. From the extract, the researchers isolated three key bioactive compounds: pinocembrin, licoflavone, and glabranin, the latter of which

demonstrated the most pronounced antioxidant activity. Subsequent investigations revealed that both licoflavone and the extract significantly reduced the expression of iNOS and COX-2, suggesting their potential application in dermatological formulations aimed at treating sensitive and inflamed skin conditions such as rosacea [39]. The aforementioned experimental and clinical evidence supporting the use of licorice in rosacea management is summarized in Table 2.

3.2. *Matricaria recutita* L. (Chamomile) Extract and Essential Oil

Matricaria chamomilla L. (synonym of *Matricaria recutita* L.) is recognized as one of the most ancient, widely applied, and well-documented medicinal plants across the globe. As mentioned by Hippocrates, Galen, and Dioscorides, the chamomile flowers were employed in the treatment of numerous medical conditions. Chamomile flowers were utilized for their anti-inflammatory properties in the management of dermatological conditions, including wounds, insect bites, ulcers, eczema, dermatitis, and burns [17,47–49]. *M. chamomilla* flowers have been extensively utilized in traditional Anatolian medicine, primarily for treating skin conditions. The usage of *M. chamomilla* flowers varied according to the method of preparation, including infusion, decoction, baths, and compresses [17,47,48]. The phenolic acids (caffeic acid, chlorogenic acid, p-coumaric acid), flavanones (apigenin, luteolin, penduletin, rutin, quercetin, and their derivatives), terpenes (α-bisabolol, bisabolol oxide A, bisabolol oxide B, β-farnesene, chamazulene, and matricin), and coumarins (umbelliferone, herniarin and 7-methoxy-coumarin) were classified as the major phytochemical constituents of the *M. chamomilla*. Chamomile flowers are rich in flavonoids, which can constitute approximately 6–9% of their composition. Among these, apigenin is recognized as one of the crucial and most biologically active constituents, serving as a key indicator of chamomile quality. According to the European Pharmacopoeia, dried chamomile flowers must contain at least 0.25% apigenin-7-glucoside to be deemed pharmaceutically acceptable. Similarly, the United States Pharmacopeia stipulates a minimum content of 0.3% apigenin-7-glucoside in dried chamomile flowers for therapeutic use. Sesquiterpene lactones, such as matricin (0.03–0.2%), and coumarins (0.01–0.08%), such as herniarin and umbelliferone, are also important phytochemical constituents of *M. chamomilla* [47,50,51]. The essential oil of *M. chamomilla* is rich in sesquiterpenes, mainly α-bisabolol (5–70%) and α-bisabolol oxide A (5–60%), α-bisabolol oxide B (5–60%), β-farnesene (7–45%), and chamazulene (1–35%) [47,50–53].

Table 2. Summary of experimental and clinical evidence supporting the use of Licorice in rosacea management.

Type of Active Extract Tested	Type of Experiment Used to Prove Activity	Active Compounds Responsible	Active Dose/Regimen	Most Probable Molecular Mechanism	Improvement Related to Rosacea	Reference
Licorice supercritical extract obtained using supercritical CO_2 with ethanol as co-solvent	In vitro antioxidant (TPC, radical scavenging assays)	Liquiritin, liquiritigenin, glycyrrhizin, isoliquiritigenin, glabridin	Concentration-dependent effects reported; antioxidant capacity correlated with total phenolic content. Highest values were 556 and 760 µmol/g for the ABTS and DPPH assay	Antioxidant activity mainly attributed to high phenolic content; free radical scavenging and redox modulation	Indirect benefit: reduction in oxidative stress, a key factor in rosacea pathophysiology	[30]
Topical formulation containing licorice-derived flavonoid	Open-label clinical study in rosacea patients (n = 62); concomitant use with topical metronidazole evaluated in a subset of participants	Licochalcone A	Once-daily topical application for 8 weeks	Anti-inflammatory and antioxidant effects; modulation of erythema-associated inflammatory pathways	Significant reduction in facial erythema; improvement in skin appearance and quality of life	[31]
Oil-in-water topical formulation containing licorice aqueous extract	Controlled clinical study in healthy volunteers; shaving- and UV-induced erythema model; complementary in vitro assays	Licochalcone A	0.025% and 0.05% (*w*/*w*) topical application, twice daily for 3 days	Potent anti-inflammatory activity via inhibition of oxidative burst in granulocytes and suppression of pro-inflammatory mediators (PGE_2, LTB_4, IL-6, TNF-α)	Significant reduction in erythema induced by UV exposure and shaving; relevant to erythema-dominant rosacea	[32]
Topical cosmetic formulation containing licorice-derived flavonoids (licochalcone A and trans-4-t-butylcyclohexanol)	Open-label, international, multicenter clinical study in subjects with sensitive, redness-prone, and rosacea-affected skin (n = 1221)	Licochalcone A; trans-4-t-butylcyclohexanol	Twice-daily topical application for 4 weeks	TRPV1 inhibition leading to reduced calcium influx in keratinocytes; anti-inflammatory and barrier-protective effects	Marked reduction in facial redness and erythema; improvement of clinical symptoms in rosacea-prone skin	[33]
Topical cosmetic skin care regimen (cleanser, day care SPF 25, night care) containing licorice-derived flavonoids (licochalcone A and trans-4-t-butylcyclohexanol)	Open-label clinical study in patients with mild to moderate rosacea subtype I (n = 32)	Licochalcone A; 4-t-butylcyclohexanol (SymSitive®)	Twice-daily topical application for 8 weeks	Anti-inflammatory effects combined with TRPV1 inhibition, leading to reduced neurogenic inflammation and improved skin barrier function	Significant reduction in erythema and skin irritation; improved skin compatibility in rosacea subtype I	[34]
Isolated chalcone compound licorice-derived	In vivo, DNCB-induced AD-like murine model (BALB/c mice, n = 6/group); in vitro THP-1 monocyte model	Isoliquiritigenin	1% (topical), once daily for 13 days	Suppression of Th2 cytokines (IL-4, IL-13) and IgE; inhibition of TNF-α, IL-6; blockade of p38α and ERK MAPK signaling	Significant reduction in erythema-associated dermatitis severity, scratching behavior, and inflammatory markers	[35]
Glabridin isolated from the hydrophobic (ethyl acetate-type) fraction of licorice extract	In vivo UVB-induced pigmentation and erythema model in guinea pigs; complementary in vitro assays	Glabridin	0.5% topical glabridin applied to UVB-irradiated skin	Inhibition of inflammatory mediators via suppression of superoxide anion production and cyclooxygenase (COX) activity	Significant inhibition of UVB-induced erythema, suggesting a potential role in redness and inflammation control	[36]

Table 2. *Cont.*

Type of Active Extract Tested	Type of Experiment Used to Prove Activity	Active Compounds Responsible	Active Dose/Regimen	Most Probable Molecular Mechanism	Improvement Related to Rosacea	Reference
Diammonium glycyrrhizinate, a glycyrrhizin salt extracted from licorice	Randomized, double-blind, placebo-controlled study in 117 rosacea patients (mainly papules and pustules)	Glycyrrhizin (as diammonium salt)	150 mg DG orally, three times daily (450 mg/day)	Anti-inflammatory and immunomodulatory: inhibits NF-κB, decreases TNF-α, IL-1, IL-6, IL-17, reduces ROS and nitric oxide synthase, increases SOD and catalase activity, protects liver cells	Enhanced reduction in papules and pustules; earlier symptom improvement, higher total effective rates (93–94% vs. 68% in standard therapy alone); allowed halving of isotretinoin and clarithromycin doses; lower incidence of adverse events (dryness, liver enzyme elevation, GI discomfort)	[37]
Topical licorice extract gel (standardized based on glycyrrhizinic acid, 20% in extract, 19.6% in gel)	Double-blind clinical trial in patients with atopic dermatitis (30 patients/group, 2-week study); compared 1% and 2% gels with base gel	Glycyrrhizinic acid	1% and 2% topical gel, applied twice daily for 2 weeks	Anti-inflammatory and antioxidant; reduces cytokine-mediated inflammation in skin; reduces erythema, edema, and pruritus	2% gel more effective than 1% in reducing erythema, edema, and itching; implies potential to reduce inflammation and erythema in rosacea	[25]
Glycyrrhetinic acid (licorice-derived metabolite)	In vitro, mast cells co-cultured with Swiss 3T3 fibroblasts	Glycyrrhetinic acid	Glycyrrhetinic acid at 50 μM strongly inhibited histidine decarboxylase activity (~80% inhibition) in mast cells	Direct inhibition of histidine decarboxylase (HDC) activity → decreased histamine synthesis; reduced maturation of mast cells; downregulation of nPKCδ mRNA expression, suggesting signaling modulation	Potential to reduce mast cell–mediated inflammation and histamine-related vasodilation/erythema in rosacea by suppressing histamine synthesis and inflammatory mediator release	[38]
Licorice leaf ethanol 96% extract	In vitro, LPS-stimulated RAW 264.7 macrophages; anti-inflammatory and antioxidant assays; NF-kB/MAPK pathway analysis	Pinocembrin, licoflavone, and glabranin	12.5–50 μg/mL (dried leaf ethanol extract, UAE); Licoflavanone: 10–200 μM, IC_{50} = 37.68 μM	Inhibition of NF-kB nuclear translocation; suppression of MAPK phosphorylation (ERK1/2, JNK, p38); reduction in iNOS, COX2, TNF-α, IL1-β, and IL-6 expression; antioxidant activity	Expected reduction in inflammation, oxidative stress, and erythema in rosacea due to NF-kB/MAPK modulation and cytokine suppression	[39]

The anti-inflammatory, antioxidant, anti-allergenic, analgesic, antimicrobial, and antiangiogenic activities of *M. chamomilla* have been reported in the literature [47–64]. *M. chamomilla*'s diverse range of biological activities is predominantly attributed to its terpenes and flavonoids. The terpene compounds matricin, chamazulene, α-bisabolol, α-bisabolol A, and B oxides demonstrate notable anti-inflammatory, anti-allergic and antioxidant properties. They act as potent inhibitors of the cyclooxygenase (COX) and lipoxygenase pathways. These compounds inhibit the release of endogenous histamine, enhance the phagocytic function of leukocytes, and activate macrophages [47,48,54,55]. The flavonoids apigenin, luteolin, and quercetin were also shown to be potent inhibitors of histamine release [54,56,57]. *M. chamomilla* influences cutaneous microcirculatory dynamics, and this modulation, alongside its anti-inflammatory properties, contributes to the attenuation of erythema [58]. These therapeutic effects of *M. chamomilla*, particularly its beneficial impact on rosacea, have been documented in the literature. Recent studies have demonstrated the efficacy of topical formulations in managing atopic dermatitis and skin irritation. One particular study found that the *M. chamomilla*-included formulation's anti-inflammatory effect in moderate eczema was comparable to that of 0.25% hydrocortisone. Moreover, clinical symptoms commonly observed in rosacea—such as pruritus, erythema, and desquamation—were markedly alleviated [59]. In another study, a cream formulation called Kamillosan (R), which contains chamomile ethanolic extract as an active ingredient (2% concentration), was shown to improve atopic eczema by Patzelt-Wenczler and Ponce-Pöschl. In the clinical study involving patients with moderate atopic eczema, Kamillosan® cream was compared to 0.5% hydrocortisone cream. Following a two-week treatment period, Kamillosan® demonstrated a mild superiority over 0.5% hydrocortisone [60]. In 2017, with the patent number "CN107397876," chamomile extract granules and capsules orally administered (10 g, three times a day) and ointment (10 g, once a day) topically applied (10–100 mg/mL) were used in clinical trials with rosacea sufferers (n = 700) and preclinical studies in mice (n = 210), and demonstrating its ability to improve microcirculation, promote skin whitening and nutrition, and act as therapy in the treatment of rosacea [61]. The lyophilized aqueous extract of *M. chamomilla* (at 7% concentration) improved atopic dermatitis-like lesions in an in vivo murine model, as shown by Ortiz-Bautista et al. [62]. The anti-inflammatory mechanism of *M. chamomilla* essential oil was determined by Chen et al. The results indicate that *M. chamomilla* essential oil suppresses inflammation in HaCaT keratinocytes stimulated by IL-22 and TNF-α. This anti-inflammatory effect is potentially mediated through the inhibition of hyperactivation and crosstalk between the PI3K/Akt/mTOR and p38 MAPK signaling pathways. Additionally, the *M. chamomilla* essential oil alleviated skin damage in an imiquimod-induced psoriatic-like murine model by downregulating pro-inflammatory cytokine expression. These findings highlight the therapeutic potential of *M. chamomilla* in the management of inflammatory dermatological conditions, including psoriasis, dermatitis, and rosacea [63]. Furthermore, *M. chamomilla* essential oil's major compound, α-bisabolol, is also particularly notable for its anti-inflammatory properties. α-bisabolol's strong anti-inflammatory activity via inhibition of 5-lipoxygenase (5-LOX) was demonstrated by an in vitro study conducted by Baylac et al. [64]. The above-mentioned experimental and clinical evidence supporting the use of chamomile in rosacea management is presented in Table 3.

Table 3. Summary of experimental and clinical evidence supporting the use of chamomile in rosacea management.

Type of Active Extract Tested	Type of Experiment Used to Prove Activity	Active Compounds Responsible	Active Dose/Regimen	Most Probable Molecular Mechanism	Improvement Related to Rosacea	Reference
Kamillosan® cream (topical cream containing 2% ethanolic extract of chamomile flowers)	Randomized, partially double-blind, half-side comparison clinical trial in patients with moderate atopic eczema: Kamillosan® vs. 0.5% hydrocortisone cream vs. vehicle cream	Chamomile phytoactives (likely bisabolol, chamazulene, apigenin, and other flavonoids/sesquiterpenes)—principal anti-inflammatory constituents of chamomile extract	Topical application twice daily for 2 weeks; cream with 2% chamomile extract compared mainly with 0.5% hydrocortisone cream	Anti-inflammatory and anti-pruritic effects via modulation of inflammatory mediators; reduction in local inflammatory response in skin; inhibition of pro-inflammatory enzymes and cytokine pathways	Mild superiority over 0.5% hydrocortisone in improving pruritus, erythema, and desquamation, symptoms common to rosacea inflammatory presentations	[60]
Chamomile extract granules/capsules and ointment	Clinical trial (rosacea patients, n = 700) + preclinical study in mice (n = 210)	Bisabolol, chamazulene, apigenin	Oral: 10 g, 3×/day; topical ointment: 10 g, 1×/day, concentration 10–100 mg/mL	Improvement of microcirculation, skin nutrition, anti-inflammatory, and soothing effects	Reduced erythema, improved skin appearance, enhanced skin nutrition and microcirculation	[61]
Lyophilized aqueous extract of *Matricaria chamomilla* (7%) in an emollient vehicle	In vivo murine model of atopic dermatitis-like lesions (BALB/c mice, n = 12)	Apigenin (major), caffeic acid (minor) identified by HPLC	Topical application: 7% extract in petrolatum, 1×/day, 6 days/week for 4 weeks	Anti-inflammatory, antioxidant, immunomodulatory effects; reduction in epidermal hyperplasia and leukocyte infiltration	Histopathological improvement of lesions (50% of mice showed lesion normalization), reduction in epidermal inflammation, potential correlation with rosacea-associated erythema and inflammation	[62]
Chamomile essential oil	In vitro: HaCaT keratinocytes stimulated with IL-22/TNF-α/LPS; in vivo: IMQ-induced psoriatic-like skin inflammation in mice	Azulene (~88.9%), Isocaryophillene (13.82%), Cedrene (10.37%), Bisabolol, other sesquiterpenes, and monoterpenes	In vitro: 30–60 μg/mL; In vivo: 16 mg/time/mice, topical twice daily for 7 days	Downregulation of PI3K/Akt/mTOR and p38MAPK pathways; inhibition of inflammatory cytokines (IL-1β, IL-6, TNF-α, IL-10, TGF-β)	Reduced erythema, scaling, and epidermal thickening; anti-inflammatory effects that could improve rosacea-related skin inflammation	[63]
Chamomile essential oil (α-bisabolol-rich)	In vitro 5-LOX inhibition	α-Bisabolol	$IC_{50} \approx 10–30$ ppm	5-lipoxygenase inhibition → anti-inflammatory	Potential, based on anti-inflammatory activity	[64]

3.3. Rosa canina L. (Rosehip, Dog Rose) Seed Oil

Rosa canina L. fruits/seeds have been utilized in traditional medicine for centuries. The rosehip, also recognized as a pharmacopoeial raw material, is commonly employed as a source of vitamins in therapeutic applications. Pliny the Elder was the first to document the medicinal properties of *R. canina* fruits/seeds after observing their use by French ethnic groups in the treatment of dog bites. This specific usage led to the plant also led to the plant being named "dog rose" [66]. Rosehip, which grows naturally across various regions of Anatolia, has long been used in traditional medicine for the management of wounds, scarring, itching, and eczema. Historical records indicate that rosehip was also included in medical prescriptions for disease treatment during the Ottoman age. The seed oils prepared from the rosehips were used to treat skin diseases such as wounds, burns, eczema, and psoriasis [66,67]. The seed oil of *R. canina* is widely used as a cosmetic ingredient. In skincare applications, rosehip oil functions as an emollient and serves as an active ingredient in formulations with anti-wrinkle, moisturizing, anti-acne, skin-soothing, depigmenting, anti-scar, and anti-stretch mark properties [67,68]. Unsaturated fatty acids (α-linolenic, linoleic, and oleic acids), phytosterols (β-sitosterol, campesterol, stigmasterol, Δ5 avenasterol, and Δ7 avenasterol), tocopherols (α-, γ-, and δ-tocopherol), carotenoids (β-carotene, lycopene, zeaxanthin, and lutein), and polyphenolic compounds (methyl esters of p-coumaric acid, vanillic acid and 4-hydroxybenzoic acid) were detected as the major phytochemicals of *R. canina* seed oil [67–76]. The major components of *R. canina* seed oil were detected as linoleic acid (25–55%), α-linolenic acid (5–35%), and oleic acid (4–25%) unsaturated fatty acids; these compounds were attributed to the high antioxidant and anti-inflammatory activities of the oil. The minor saturated fatty acids present in rosehip seed oil, palmitic acid (1–10%) and stearic acid (0–3%), contribute to its emollient characteristics as well as its function as a stabilizing and thickening agent in formulations [68–73]. Moreover, carotenoids—particularly β-carotene—are abundantly present in rosehip seed oil. As demonstrated by Fromm et al., *β*-carotene effectively mitigates the oxidation of polyunsaturated fatty acids through multiple mechanisms, including quenching of reactive oxygen species, light filtering, inactivation of excited sensitizers, and free radical scavenging [73,74]. From a dermatological perspective, carotenoids such as lycopene and *β*-carotene also contribute to skin health not only by mitigating oxidative stress but also by promoting collagen synthesis, a critical process for preserving skin elasticity and firmness [75]. Total phytosterol, tocopherol and carotenoid contents of the cold-pressed rosehip seed oil were analyzed as 6485.4, 1124.7, and 107.7 mg/kg, respectively, by Grajzer et al. β-sitosterol was detected to be the main sterol, making up ca. 80.5% of the total sterols (5297.3 ± 311.6 mg/kg). The tocopherol contents were detected as γ-tocopherol (777.1 ± 9.3 mg/kg), δ-tocopherol (230.4 ± 1.3 mg/kg), and α-tocopherol (116.6 ± 6.2 mg/kg). Furthermore, the total phenolic content identified in rosehip seed oil reached up to 783.55 µg/kg, with p-coumaric acid methyl ester being the dominant compound, accounting for as much as 391.77 µg/kg [76]. Anti-inflammatory, antioxidant, antimicrobial, and anti-aging activities of the *R. canina* seed oil were determined in the literature. Because of these activities, rosehip seed oil exhibits therapeutic potential in the management of various skin conditions, including rosacea. Its efficacy is largely attributed to its rich composition of fatty acids, carotenoids, and phytosterols, which collectively contribute to skin regeneration and repair. Owing to these bioactive compounds, the oil functions as a natural skincare agent with moisturizing and skin-rejuvenating properties [66–81]. There are no studies in the literature that specifically investigate the direct effects of *R. canina* seed oil on rosacea. However, due to its rich phytochemical composition and potent antioxidant and anti-inflammatory activities, rosehip seed oil holds considerable potential for rosacea. This review aims to offer insights that may guide and stimulate future investigations on

the subject. The linoleic and α-linolenic acids abundant in *R. canina* seed oil contribute to anti-inflammatory activity via the inhibition of cyclooxygenase COX-1 and COX-2, as shown by Winther et al. In this manner, it may help alleviate the redness and tenderness commonly occurring with rosacea by modulating inflammatory responses and reinforcing the skin barrier [77]. Previous studies have also shown that oils derived from *R. canina* are rich in fatty acids, particularly linoleic, α-linolenic, and oleic acids, which are known to contribute to wound-healing processes. These fatty acids are capable of enhancing cell membrane permeability, thereby facilitating the entry of growth factors and promoting cellular proliferation, migration, and neoangiogenesis. As a result, they play a direct role in the proliferative phase of wound healing. In addition, they aid in maintaining dermal structure and stimulate fibroblast activity, a key factor in collagen production. Rosehip oil has been shown to activate type III collagen and enhance collagen synthesis, thereby promoting wound contraction and tissue repair. These effects are likely mediated by the oil's antioxidant properties, which protect skin cells from oxidative stress-induced collagen degradation, ultimately supporting skin integrity and elasticity [75,78,79]. Pereira Oliveira et al. have investigated nanoemulsions containing sunflower oil (15%, *w*/*w*) and rosehip oil (3%, *w*/*w*) combined with different synthetic emulsifiers (designated as Nano-1 and Nano-2) for their cellular uptake and in vitro cytotoxicity on fibroblasts (NIH-3T3) and keratinocytes (HaCaT). Nano-2 exhibited no cytotoxic effects on either cell type after 24 and 48 h of incubation. In contrast, Nano-1 significantly reduced cell viability by 38% in NIH-3T3 and 51% in HaCaT cells. Both formulations were also evaluated for their wound-healing efficacy in ex vivo ulcer models. Compared to the control group, both nanoemulsions enhanced the healing rate, with Nano-1 showing a notably faster healing response despite having the same oil composition as Nano-2. This suggests improved skin permeability and active compound delivery to the epidermal layer. Consequently, both nanoemulsions—particularly Nano-1—hold potential for use in wound care and may also offer therapeutic benefits in dermatological conditions such as psoriasis, rosacea, and atopic dermatitis [80]. In a study by Oargă et al., the effects of topical *R. canina* seed oil on facial skin parameters in 20 female volunteers over 8 weeks were investigated. The treatment significantly reduced the appearance of wrinkles, UV-induced spots, and erythema. Improvements were assessed using skin imaging analysis and participant feedback. The results suggest that rosehip oil, rich in antioxidants like unsaturated fatty acids and phenolic compounds, supports skin regeneration and barrier protection. These findings highlight its potential as a supportive cosmetic ingredient, especially for conditions involving redness and inflammation, such as rosacea [75]. To date, the literature lacks studies explicitly evaluating the effects of *R. canina* seed oil on rosacea. Nevertheless, given its proven antioxidant and anti-inflammatory properties across a range of dermatological conditions, it may serve as a promising candidate in rosacea management. The experimental and clinical evidence discussed above regarding the use of rosehip in rosacea management is presented in Table 4.

Table 4. Summary of experimental and clinical evidence supporting the use of rosehip in rosacea management.

Type of Active Extract Tested	Type of Experiment Used to Prove Activity	Active Compounds Responsible	Active Dose/Regimen	Most Probable Molecular Mechanism	Improvement Related to Rosacea	Reference
Rosehip seed oil (topical)	In vivo study on 20 female volunteers; 8-week treatment; facial skin imaging analysis and participant feedback	Unsaturated fatty acids (linoleic acid, alpha-linolenic acid) and phenolic compounds	Topical application once daily for 8 weeks	Antioxidant activity, anti-inflammatory effects, support of skin regeneration and barrier protection	Reduced erythema, improved barrier function; potential benefit for rosacea due to anti-inflammatory and redness-mitigating effects	[75]
Nanoemulsions containing rosehip oil (3% *w*/*w*) + sunflower oil (15% *w*/*w*) with synthetic emulsifiers (Nano-1 and Nano-2)	In vitro: NIH-3T3 fibroblasts, HaCaT keratinocytes; Ex vivo: human skin explants (hOSEC); Confocal microscopy penetration studies; Cytokine release assay	Rosehip oil bioactives (unsaturated fatty acids, phenolics, carotenoids)	Nano-1: 6.5×10^{13}–3.2×10^{11} particles/mL; Nano-2: 3.2×10^{11} particles/mL; daily application for 7–14 days (ex vivo wound healing)	Improved delivery of bioactive compounds through skin layers; modulation of keratinocyte and fibroblast uptake; no induction of pro-inflammatory cytokines (IL-6, TNF-α)	Enhanced skin barrier penetration, improved wound closure, non-inflammatory profile suggesting potential for rosacea management by reducing irritant-induced inflammation	[80]
Rosehip powder	In vitro assays on human peripheral blood leukocytes (LPS/IFN-γ stimulated) and primary chondrocytes (IL-1β stimulated)	Ursolic acid, betulinic acid, galactolipids (GLGPG), DHA, α-tocopherol	Tested at μg/mL concentrations in cell culture; effects seen from ~10–100 μg/mL depending on cytokine	Downregulation of pro-inflammatory chemokines/cytokines (CCL5/RANTES, CXCL10/IP-10, IL-6, IL-12), decreased MMPs (MMP 1,3,13) and ADAMTS-4 expression	Anti-inflammatory potential via reduced cytokine/chemokine release and gene expression; theoretical benefit for rosacea inflammation and erythema	[82]
Rosehip seed oil	In vitro antioxidant assays (ABTS and DPPH radical scavenging)	Polyphenols, tocopherols (vitamin E), carotenoids, unsaturated fatty acids	DPPH $IC_{50} \approx 0.150$ mg/mL; ABTS antioxidant capacity ≈ 0.215–0.269 μmol/mL (pure oil)	Free radical scavenging; lipid peroxidation inhibition; antioxidant defense	May reduce oxidative stress and inflammation in rosacea-affected skin by neutralizing ROS and protecting cells from oxidative damage	[83]

3.4. Hypericum perforatum L. (St. John's Wort) Macerated Oil

St. John's wort oil, an oily extract derived from the flowering aerial parts of *Hypericum perforatum* L., represents one of the oldest traditional medicinal preparations, widely utilized in Türkiye and across various European traditional medicine systems [85]. Dermatological applications of *H. perforatum* macerated oil have been documented throughout history, reflecting its longstanding role in traditional medicine. First-century Greek medical authorities such as Galen, Dioscorides, Pliny, and Hippocrates utilized the wound-healing efficacy of St. John's wort oil in their therapeutic practices. One of the first documented references to the medicinal use of this oil appears in *Naturalis Historiae* by Pliny the Elder (23–79 A.D.) The medicinal use of St. John's wort persisted throughout the Middle Ages, with 16th-century herbalists such as Paracelsus, Gerard, and Culpeper advocating its preparations for wound healing and pain relief [86,87]. A wide range of topical uses for St. John's wort are documented in both traditional and scientific sources, including the treatment of minor wounds, sunburn, blunt injuries, ulcers, varicose veins, hemorrhoids, muscular pain, rheumatism, cramps, pressure ulcers, keloid scars, and post-extraction dental care. These applications are grounded in traditional practices, clinical observations, and, in some cases, the doctrine of signatures—which posited that the plant's perforated leaves symbolized its capacity to heal wounds. The British Pharmacopoeia endorses its use in managing wounds, cuts, and various skin and mucosal injuries. Furthermore, the German Commission E has approved its topical application for both the treatment and aftercare of acute and blunt injuries [88]. Recent studies have sporadically explored the therapeutic potential of *H. perforatum* in conditions such as wound healing, atopic dermatitis, psoriasis, and herpes simplex, employing refined active compounds and advanced dermatological delivery systems [85–95]. The phytochemical profile of *H. perforatum* oil includes multiple groups of active substances, particularly naphthodianthrone derivatives (hypericin and pseudohypericin), acylated phloroglucinols (hyperforin and adhyperforin), as well as a diverse range of flavonoids like quercetin, quercitrin, hyperoside, rutin, kaempferol, biapigenin, and amentoflavone [85–92]. The strongly lipophilic compound hyperforin, a phloroglucinol derivative, was identified at approximately 0.6% in freshly prepared *H. perforatum* oil [92]. In a study conducted by Orhan et al., twenty-one samples of both traditionally prepared and commercially produced St. John's wort macerated oils were analyzed using LC-DAD-MS. Pseudohypericin and hypericin were detected in all samples at concentrations ranging from 0.135 to 3.280 μg/g and 0.277 to 6.634 μg/g, respectively. Chlorogenic acid was measured in only one sample (1.063 μg/g), while hyperforin and adhyperforin were identified in four (0.977–2.399 μg/g) and six samples (0.005–3.165 μg/g), respectively [90]. The therapeutic effectiveness of *H. perforatum* oil in dermatological disease is likely attributed to its antioxidant, antimicrobial, and anti-inflammatory properties, along with its ability to promote fibroblast migration, enhance collagen synthesis, and support keratinocyte differentiation. The naphthodianthrones (e.g., hypericin) and phloroglucinols (e.g., hyperforin) compounds contribute to the oil's therapeutic activity [85–92]. In the context of rosacea, the extraction of the *H. perforatum* plant with olive oil confers synergistic benefits; the virgin olive oil is effective in managing a range of dermatological conditions such as xerosis, rosacea, psoriasis, atopic and contact dermatitis, eczema (including severe hand and foot eczema), seborrhea, pruritus, and various inflammatory dermatoses. The therapeutic efficacy of olive oil in these disorders is largely attributed to its pronounced anti-inflammatory and antioxidant activities, mediated by bioactive compounds such as oleuropein, oleocanthal, and hydroxytyrosol. Additionally, olive oil has shown promising effects in promoting wound healing and protecting skin from ultraviolet-induced damage [96]. Recent investigations have underscored the therapeutic value of *H. perforatum* macerated oil in treating dermatological conditions characterized by chronic inflammation, microbial dysbiosis, and

impaired tissue repair—features shared with rosacea. A landmark clinical study involving idiopathic granulomatous mastitis patients reported a 94% overall success rate following twice-daily topical application of *H. perforatum* oil over six weeks. Significant amelioration in erythema, scaling, induration, and ulceration was observed ($p < 0.001$), indicating strong anti-inflammatory and regenerative effects [93]. In a controlled animal study using excisional wounds in rats, it was understood that the *H. perforatum* oil led to rapid wound area reduction (≈97% closure by day 11), enhanced angiogenesis, collagen deposition, and fibroblast infiltration, surpassing standard treatments such as mupirocin and Vaseline [94]. A bioanalytical investigation employing LC-FTMS profiling demonstrated that *H. perforatum* oil macerates (Oleum Hyperici), traditionally used in Kosovo, consistently contain hyperforin, a prominent phloroglucinol derivative known for its antimicrobial and anti-biofilm properties. Functionally, the Kosovar Hypericum oil macerates demonstrated notable inhibitory effects on *Staphylococcus aureus* biofilm formation, with $MBIC_{50}$ values ranging from 0.004% to 0.016% v/v, alongside moderate quorum-sensing inhibitory activity ($QSIC_{50}$ range: 0.064–0.512% v/v). These properties are particularly relevant to rosacea management, as *S. aureus* colonization and biofilm development are known to contribute to inflammatory exacerbations in rosacea-prone skin [89]. A randomized, double-blind, placebo-controlled clinical study by Schempp et al. evaluated the efficacy of a topical cream containing 5% of an apolar extract—for which the extraction process was performed with supercritical carbon dioxide as the eluting agent—of St. John's wort in the treatment of atopic dermatitis. In this split-body design trial involving 20 patients, the St. John's wort cream was applied to one side of the body and a placebo to the other over a period of four weeks. The results demonstrated a significant reduction in SCORAD scores on the side treated with the *H. perforatum* cream, indicating notable improvement in inflammation and clinical symptoms. Histological analysis revealed a decrease in epidermal thickness and inflammatory cell infiltration, alongside a marked reduction in TNF-α expression in the treated areas. These findings highlight the therapeutic potential of *H. perforatum* in managing inflammatory skin diseases. Given the shared inflammatory mechanisms, including elevated pro-inflammatory cytokines and vascular dysregulation, between atopic dermatitis and rosacea, *H. perforatum* oil may represent a promising topical treatment option for rosacea as well [95]. Considering the shared pathophysiological features between rosacea and these dermatological conditions—namely chronic inflammation, impaired barrier function, and vascular dysregulation—*H. perforatum* macerated oil may represent a valuable adjunctive approach in rosacea management. These findings warrant future randomized clinical trials specifically targeting rosacea to further elucidate its therapeutic role. Table 5 presents the experimental and clinical evidence related to the use of St. John's Wort in rosacea management.

Table 5. Summary of experimental and clinical evidence supporting the use of St. John's wort in rosacea management.

Type of Active Extract Tested	Type of Experiment Used to Prove Activity	Active Compounds Responsible	Active Dose/Regimen	Most Probable Molecular Mechanism	Improvement Related to Rosacea	Reference
St. John's wort oil macerate	In vitro biofilm inhibition assay, quorum-sensing inhibition assay against *Staphylococcus aureus*	Hyperforin (phloroglucinol derivative)	$MBIC_{50}$ (biofilm inhibition): 0.004–0.016% *v*/*v*; $QSIC_{50}$ (quorum-sensing inhibition): 0.064–0.512% *v*/*v*	Anti-biofilm, quorum-sensing inhibition; reduces bacterial attachment, virulence, and biofilm formation; hyperforin also has anti-inflammatory properties	Limits *S. aureus* colonization and biofilm-mediated inflammatory triggers on skin; may reduce erythema, inflammation, and irritation in rosacea-prone skin; supports overall skin barrier protection and microbial balance	[89]
St. John's wort oil macerate (topical oil massage)	Clinical case series on 21 women with idiopathic granulomatous mastitis-associated persistent skin lesions (pre- vs. post-treatment assessment)	Hypericin, hyperforin, and fatty acids	Topical massage twice daily for 2 min for 6 weeks (after standard steroid/antibiotic therapy)	Anti-inflammatory and wound-healing effects via reduction in hyperaemia, scaling, induration, and ulceration (skin lesion regression); may involve modulation of inflammatory response and enhancement of tissue repair mechanisms	Very significant regression of persistent skin lesions (overall success rate ~94%; total clearance + decreased severity) suggests potential to reduce chronic inflammation and erythema—relevant to rosacea inflammation control	[93]
St. John's wort oil macerate	In vivo—excision wound model in male Sprague Dawley rats	Hypericin, hyperforin, flavonoids, fatty acids	Topical application on wound site once daily	Anti-inflammatory, antioxidant, and tissue regeneration effects: reduces pro-inflammatory cytokines, enhances collagen deposition, promotes angiogenesis and epithelialization	Accelerated wound closure, reduced inflammation, improved tissue repair; suggests potential benefit in rosacea-like inflammation and erythema due to anti-inflammatory and healing properties	[94]
H. perforatum apolar extract obtained by supercritical CO_2 extraction, formulated as a topical cream	Randomized, double-blind, placebo-controlled half-side (split-body) clinical trial; additional histological and immunohistochemical evaluation	Predominantly hyperforin (lipophilic phloroglucinol derivative enriched by CO_2 extraction); other apolar constituents	5% *H. perforatum* extract in cream; applied to one body side vs. placebo on contralateral side for 4 weeks; n = 20 patients with atopic dermatitis	Anti-inflammatory effect via significant reduction in TNF-α expression, decreased inflammatory cell infiltration, and reduced epidermal hyperplasia; modulation of cytokine-mediated skin inflammation	Reduction in erythema and inflammatory severity; suppression of pro-inflammatory cytokines relevant to rosacea pathophysiology (TNF-α–driven inflammation and vascular responses), suggesting potential benefit for rosacea-associated redness and inflammation	[95]

3.5. Calendula officinalis L. (Marigold) Macerated Oil

Calendula officinalis L. (marigold) flower macerated oil has been traditionally employed in medicinal practices since antiquity, particularly for the management of wounds and various dermatological ailments. Historical records indicate that the use of *C. officinalis* flowers for their soothing effects can be traced back to the 12th century [98,99]. Ethnobotanical studies conducted in Türkiye have documented the use of *C. officinalis* in the treatment of psoriasis. *C. officinalis* flowers are used externally in the form of a cream for eczema and psoriasis [100–102]. According to the Committee on Herbal Medicinal Products (HMPC) of the European Medicines Agency (EMA), *C. officinalis* flower-based medicinal products are indicated for skin and mucosal inflammations, as well as minor wounds, within the context of traditional herbal medicinal use [99]. Owing to its well-documented tolerability, the plant is widely utilized in cosmetic formulations targeting sensitive skin and soothing applications (e.g., after-sun products) and is included in various dermatological preparations [103]. *C. officinalis* macerated oil contains a complex mixture of bioactive compounds; triterpenoids—specifically triterpene alcohols and triterpene saponins such as faradiol, taraxasterol, and lupeol, along with their esters (e.g., faradiol-3-palmitate and faradiol-3-myristate)—are present and known for their anti-inflammatory properties. Carotenoids such as lutein, β-carotene, flavoxanthin, and rubixanthin impart the deep orange coloration of the oil and offer further antioxidant and anti-inflammatory benefits. Additionally, flavonoids like quercetin, isorhamnetin, and kaempferol derivatives are present, contributing antioxidant and skin-soothing effects [98,104–106]. Furthermore, topical application of virgin olive oil has been supported by randomized controlled trials showing its protective, moisturizing, and elasticity-enhancing effects in skin barrier maintenance. Within this context, using virgin olive oil as a carrier in *C. officinalis* macerated oil enhances its antioxidant and anti-inflammatory potential, which could be relevant for mitigating cutaneous inflammation observed in rosacea [107,108]. While no clinical trials currently exist evaluating *C. officinalis* macerated oil in the treatment of rosacea directly, several clinical and experimental studies have demonstrated that it has antioxidant, antimicrobial, anti-inflammatory, and wound-healing properties with potential in the treatment of rosacea. In one study, the anti-inflammatory effects of *C. officinalis* flower extract were prepared via maceration in refined soy oil, stabilized with tocopherol, were investigated. In vitro experiments using RAW 264.7 macrophage cells demonstrated that the extract significantly inhibited lipopolysaccharide (LPS)-induced nitric oxide (NO) production in a dose-dependent manner without causing cytotoxicity. These findings indicate the extract's capacity to modulate key inflammatory mediators involved in skin inflammation. The oil-based extract also showed antioxidant properties attributed to its bioactive compounds, such as flavonoids and triterpenoids. By mitigating inflammatory responses and protecting against oxidative damage, *C. officinalis* macerate may contribute to reducing inflammation and improving skin barrier function in rosacea patients [99]. Pommier et al. conducted a randomized clinical trial to evaluate the efficacy of a *C. officinalis* flower lipophilic ointment (Pommade au *Calendula* par Digestion; petrolatum-based digestion, non-solvent extract) in preventing acute dermatitis caused by radiation therapy in breast cancer patients. The study compared the *C. officinalis* ointment to a standard trolamine-based treatment. It was shown that the *C. officinalis* ointment significantly reduced the incidence of grade 2 or higher acute radiation dermatitis compared to the control group [109]. In another study, which was conducted by Sharifi-Heris et al., the effects of 1.5% *C. officinalis* ointment and 1.5% olive oil ointment on diaper dermatitis in infants under two years old were compared. Over seven days, both treatments significantly reduced erythema and lesion severity, with no statistically significant difference between the two groups. Importantly, neither ointment caused adverse effects, highlighting their safety and tolerability in sen-

sitive skin. Although this study targeted diaper dermatitis, its findings have relevance for rosacea, another chronic inflammatory skin condition characterized by erythema and skin sensitivity. The demonstrated anti-inflammatory and soothing effects of *C. officinalis* ointment suggest potential benefits in alleviating rosacea symptoms such as facial redness and irritation. Furthermore, the safety profile observed in sensitive infant skin supports the suitability of calendula ointment as a gentle topical option for managing rosacea-prone skin [110]. In a study carried out by Okuma et al., lamellar gel phase (LGP) emulsion incorporating 15% *C. officinalis* oil was formulated, and the therapeutic potential was assessed in a rat wound model. The results of the in vivo studies indicated that the LGP emulsion (administered at 15 mg/mL) transiently elevated leukocyte infiltration during early wound healing (days 2 and 7) but subsequently reduced inflammatory cell presence by days 14 and 21 relative to control wounds. Moreover, early collagen deposition was attenuated, while re-epithelialization was accelerated, indicating that the formulation effectively enhanced the regenerative phase of wound repair. The demonstrated biphasic immunomodulatory activity of the calendula oil LGP emulsion—initially promoting controlled leukocyte recruitment followed by reduced inflammation—suggests potential benefit in tempering excessive inflammation typical in rosacea. Furthermore, the accelerated re-epithelialization observed in treated wounds may parallel enhancements in barrier repair and epidermal integrity, critical for reducing rosacea symptoms such as persistent redness, papules, and barrier dysfunction [111]. Table 6 provides a summary of the experimental and clinical studies evaluating the role of marigold in rosacea management.

3.6. *Rosa damascena* Miller (Damask Rose) Essential Oil

Rosa damascena Miller is a hybrid species derived from the cross between *Rosa gallica* L. and *Rosa phoenicia* Boiss [113]. *R. damascena*, commonly known as the Damask rose, is a perennial, bushy shrub and stands as the most renowned ornamental species within the Rosaceae family globally, particularly valued in the perfumery and food sectors and for medicinal purposes [114]. The cultivation of *R. damascena* and the production of its derived products constitute a substantial component of the agricultural economies in Bulgaria and Türkiye, while also holding regional significance in various areas of the Middle East and the eastern Mediterranean [115]. An average of 15,000–16,000 tons of rose flower oil are produced annually worldwide. Approximately 90% of global rose flower oil production is produced by Türkiye and Bulgaria [116]. In Türkiye, nearly all of the production areas are located in Isparta, Afyon, Burdur, and Denizli. Isparta and its surrounding area, in particular, have become not only Türkiye's but also the world's leading rose flower oil production center [116,117]. The extraction of damask rose essential oil through distillation likely originated in Persia during the late 7th century AD and was subsequently developed in the provinces of the Ottoman Empire. For an extended period, the damask rose flowers have played a crucial role in traditional formulations, especially for their anti-inflammatory and wound-healing properties [114–117]. Medicinal preparations and pastes derived from *R. damascena* oil were widely utilized in the Ottoman Empire. In Edirne, the empire's second capital, roses were cultivated in an area known as Gülhane within the palace grounds. Rose oil was commonly employed in traditional medicine and was specifically used to treat skin diseases such as eczema [118,119]. In addition, over a millennium ago, Avicenna (980–1037 AD) documented the diverse medicinal properties of the damask rose, highlighting its ability to heal skin and mucosal lesions, as well as its anti-nociceptive and anti-inflammatory effects [114]. The essential oil derived from *R. damascena* flowers is distinguished by its high content of monoterpene alcohols, predominantly citronellol (20–34%), geraniol (5–22%), and nerol (5–12%), along with notable amounts of phenylethyl alcohol (~2.5%) and linalool (~1%). In addition to these compounds, aliphatic hydrocarbon

compounds such as nonadecane (8–15%), heptadecane (1–2.5%), and heneicosane (3–5.5%) are also present in the oil. Citronellol constitutes the principal component of rose oil and serves as a key determinant of its quality. The amount of citronellol in damask rose essential oils produced in Türkiye exceeds the 20% to 34% range accepted by international quality standards, and although it varies depending on harvest time, production method, and storage conditions, it is reported to be between 25% and 45% [113,114,120–123]. *R. damascena* essential oil, in addition to its past use in traditional medicine for skin disorders, holds promise for its potent anti-inflammatory, antimicrobial, antioxidant, and anti-aging activities in rosacea [113–126]. The protective effects of *R. damascena* essential oil against UVB-induced oxidative stress and photoaging in a rat model were investigated by Abdallah et al. UVB exposure was used to induce skin damage characterized by increased oxidative markers, elevated matrix metalloproteinases (MMPs) expression, and activation of mitogen-activated protein kinase (MAPK) signaling pathways. Topical administration of *R. damascena* essential oil nanoemulsion significantly attenuated oxidative damage by reducing reactive oxygen species levels and lipid peroxidation in the skin. The demonstrated antioxidant and anti-inflammatory properties of *R. damascena* essential oil, along with its regulatory effects on MAPK and MMP pathways, suggest potential therapeutic benefits in managing rosacea symptoms [124]. In a study that was carried out by Mohsen et al., the *R. damascena* methanolic extract's in vitro anti-collagenase activity, effectively inhibiting collagen-degrading enzymes, was demonstrated. In the study by Mohsen et al. (2020) [125], the essential oil obtained from *Rosa damascena* Mill. flowers was analyzed using solid-phase microextraction gas chromatography–mass spectrometry (SPME–GC–MS) to characterize its volatile metabolite profile in relation to skin anti-aging potential. The essential oil was found to be rich in monoterpenes and oxygenated monoterpenes, with major constituents including citronellol, geraniol, nerol, and phenylethyl alcohol, compounds well known for their antioxidant and skin-protective properties. While the study primarily focused on the anti-collagenase activity of methanolic extracts, the essential oil was discussed as a biologically relevant fraction contributing to the overall dermatological value of *R. damascena*. The volatile profile supports the traditional and cosmetic use of rose oil in skin care formulations, particularly in the prevention of collagen degradation and photoaging, although direct in vitro anti-collagenase IC_{50} values were not determined for the essential oil fraction in this study. *R. damascena* oil may help alleviate structural skin damage, minimize visible vascular changes, and improve overall skin resilience in rosacea patients [125]. In an experimental study, a traditionally used polyherbal formulation's wound-healing effects in a burn wound model in rats were evaluated. The formulation included aqueous extracts of *Solanum nigrum* L., *Malva sylvestris* L., and *R. damascena* essential oil. Topical application to burn sites accelerated epithelialization, promoted earlier granulation tissue formation, and enhanced collagen deposition during the healing process. Histopathological analysis revealed reduced inflammatory cell infiltration, improved dermal matrix organization, and increased vascularization. These wound-healing effects were associated with elevated antioxidant capacity and suppression of pro-inflammatory mediators. The anti-inflammatory, antioxidant, and collagen-supporting properties of *R. damascena* oil may be beneficial in alleviating dermal connective tissue weakness, vascular dilation, and chronic inflammation observed in rosacea. Therefore, *R. damascena* essential oil demonstrates potential for inclusion in the composition of formulations intended for the treatment of rosacea [126]. Table 7 presents an overview of the experimental and clinical studies evaluating the use of *R. damascena* essential oil in rosacea management.

Table 6. Summary of experimental and clinical evidence supporting the use of marigold in rosacea management.

Type of Active Extract Tested	Type of Experiment Used to Prove Activity	Active Compounds Responsible	Active Dose/Regimen	Most Probable Molecular Mechanism	Improvement Related to Rosacea	Reference
Marigold extract (commercial extract in refined soybean oil, stabilized with tocopherol)	In vitro inflammation model: LPS-stimulated RAW 264.7 murine macrophages; NO production measured by Griess assay; cell viability by AlamarBlue®	Terpenoids (faradiol esters, bisabolol), flavonoids (quercetin, kaempferol, isorhamnetin), carotenoids, polyunsaturated fatty acids (calendic acid)	16–147 µL/mL; dose-dependent activity; ~50% inhibition of NO production at 147 µL/mL without cytotoxicity after 24 h incubation	Inhibition of inducible nitric oxide synthase (iNOS)-mediated NO production in activated macrophages; attenuation of LPS/TLR4-driven inflammatory signaling; indirect reduction in downstream pro-inflammatory mediators	Reduction in NO-mediated vasodilation and inflammatory signaling may alleviate erythema, flushing, and inflammatory exacerbations characteristic of rosacea; supports barrier-friendly, soothing adjunctive skincare	[99]
Marigold lipophilic ointment (Pommade au *Calendula* par Digestion; petrolatum-based digestion, non-solvent extract)	Randomized, controlled clinical trial in humans (breast cancer patients receiving adjuvant radiotherapy; n = 254)	Triterpenoid esters (faradiol monoesters), terpenoids, flavonoids (quercetin, isorhamnetin derivatives), carotenoids	Topical application to irradiated skin after each radiotherapy session throughout treatment period	Suppression of inflammatory cascade via inhibition of pro-inflammatory mediators (TNF-α, COX-2–related pathways), reduction in oxidative stress, stabilization of skin barrier and vascular response	Reduced inflammation, erythema and pain; mechanisms overlap with rosacea pathophysiology (neurovascular dysregulation, cytokine-driven inflammation), supporting potential adjunctive benefit in rosacea	[109]
Marigold ointment (1.5%) formulated in a beeswax- and lanolin-based carrier system; topical semisolid preparation	Triple-blind randomized clinical trial conducted in infants with non-severe, non-infected diaper dermatitis	Triterpenoids, flavonoids, carotenoids	Topical application of 1.5% ointment after each diaper change, for a duration of 7 days	Anti-inflammatory and antioxidant activity; enhancement of skin barrier function; reduction in erythema through modulation of inflammatory mediators	Anti-inflammatory and barrier-protective effects may be relevant to inflammatory dermatoses, including rosacea	[110]
Marigold oil formulated as a lamellar gel phase (LGP) emulsion	In vitro cytotoxicity assays (L929 fibroblasts, Annexin V/PI flow cytometry) and in vivo full-thickness excisional wound healing model in Wistar rats with histological (H&E, Gomori trichrome) and morphometric analyses	Flavonoids, triterpenoid esters, saponins, tannins, coumarins, and terpenoids	LGP emulsion containing 15% (*w*/*w*) calendula oil, applied topically once daily under occlusive dressing; in vivo dose reported as 15 mg/mL formulation; non-cytotoxic in vitro at 50–1000 µg/mL	Modulation of the inflammatory phase of tissue repair: early controlled leukocyte recruitment, followed by reduction in inflammatory infiltrate, enhanced angiogenesis, accelerated re-epithelialization, regulation of collagen deposition, and maintenance of wound hydration via lamellar structures enabling sustained release	Anti-inflammatory modulation, improved barrier restoration, reduced prolonged inflammation, and enhanced tissue repair are mechanistically relevant to rosacea, a condition characterized by impaired barrier function, chronic inflammation, and erythema	[111]

Table 7. Summary of experimental and clinical evidence supporting the use of Damask rose essential oil in rosacea management.

Type of Active Extract Tested	Type of Experiment Used to Prove Activity	Active Compounds Responsible	Active Dose/Regimen	Most Probable Molecular Mechanism	Improvement Related to Rosacea	Reference
Essential oil of *R. damascena*	In vitro cell culture assays on B16F10 murine melanoma cells: cell viability, melanin content, mushroom tyrosinase activity, ROS suppression, and tyrosinase protein level evaluation	Major volatile compounds: citronellol (~37.1%), geraniol (~12.7%), linalool, phenylethyl alcohol, and a total of 63 volatile components identified by GC–MS; oxygenated monoterpenes dominate (~56%).	Tested at 0.2–200 µg/mL in B16F10 cells; effects on melanin and ROS were significant at 2, 20, and 200 µg/mL concentrations.	Antioxidant and anti-melanogenic effects: suppression of intracellular ROS production; reduction in melanin content.	Demonstrates dose-dependent antioxidant and enzyme-modulating activities that are relevant to skin inflammation control; reduction of ROS and melanin synthesis may overlap with mechanisms beneficial in rosacea, particularly where oxidative stress and pigment-related inflammation are implicated	[123]
R. damascena essential oil formulated in an emulgel base (100 mg/g) and nano-emulgel (ROSE-NANO) at 50 mg/g and 100 mg/g for topical application	In vivo UVB-induced photoaging model in adult male Wistar rats, with topical pretreatment (0.5 g of emulgel per rat) 1 h before daily UVB exposure; evaluated via biochemical markers, histology, and gene/protein assays	Major volatile constituents: geraniol (29.2%), nerol (23.4%), citronellol (16.34%), phenylethyl alcohol (4.96%), linalool (3.24%), and others identified by GC–MS	0.5 g per rat per day topically of: (a) emulgel with 100 mg/g ROSE, (b) nano-emulgel with 50 mg/g ROSE, (c) nano-emulgel with 100 mg/g ROSE; applied 1 h before UVB irradiation	Mitigation of UVB-induced oxidative damage through enhanced catalase and superoxide dismutase activities, reduction in pro-inflammatory cytokines (IL-6, TNF-α), downregulation of MAPK signaling (JNK, ERK1/2, p38), and decreased MMP-9 expression, resulting in protection against collagen degradation	The antioxidant, anti-inflammatory, and extracellular matrix protective effects are relevant to rosacea, a chronic inflammatory skin condition involving oxidative stress, MAPK/MMP dysregulation, and inflammation	[124]
Methanolic flower extracts ERF (Expanded Rose Flowers) and URF (Unexpanded Rose Flowers) and essential oil of *R. damascena*	In vitro anti-collagenase assay (methanolic extract); chemical profiling by UHPLC–MS/MS and HS-SPME–GC–MS (essential oil)	Methanolic extract: polyphenols and flavonoids (quercetin and kaempferol derivatives); essential oil: monoterpene alcohols (citronellol, geraniol, nerol, phenylethyl alcohol)	ERF: $IC_{50} \approx 25$–30 µg/mL URF: $IC_{50} \approx 45$–50 µg/mL	Inhibition of collagenase activity and antioxidant protection of dermal extracellular matrix (extract); potential anti-inflammatory and antioxidant effects inferred for the essential oil based on its terpene composition	May help limit matrix degradation, oxidative stress, and inflammatory skin damage associated with rosacea	[125]
Polyherbal cream (PHC): aqueous extracts of *Malva sylvestris* leaves + aqueous extracts of *Solanum nigrum* leaves + *R. damascena* essential oil	In vivo second-degree burn wound healing in rats; histopathological evaluation; antioxidant (DPPH) and antimicrobial (micro-dilution) assays	Phenolic compounds and tannins in aqueous extracts; volatile compounds in essential oil	Topical application of PHC (cream with 5% aqueous extracts each, 33% oily extract in a base of eucerin/petrolatum/beeswax) daily for 14 days	Accelerates wound closure via enhanced re-epithelialization, neovascularization, and collagen deposition; antioxidant radical scavenging	Suggests potential to mitigate inflammatory and oxidative processes in chronic skin conditions like rosacea by reducing inflammation and scavenging free radicals	[126]

3.7. Origanum vulgare L. (Common Oregano) Essential Oil

Origanum vulgare L. (generally referred to as common oregano) is regarded as one of the most widely recognized species, valued both for its applications in traditional medicine and its use as a culinary spice [127]. Since approximately the 5th century B.C., dating back to the era of Hippocrates, *O. vulgare* aerial parts/leaves have been utilized for their antimicrobial properties and therapeutic role in managing dermatological infections [128]. The aerial/leaf parts of *Origanum* spp. have been frequently used in Anatolian medicine and is reported to be used for skin diseases such as skin infections, eczema, wounds, and itchy rashes [129,130]. The chemical profile of *O. vulgare* essential oil is primarily influenced by both genetic and environmental factors. This species is capable of producing chemotypes, with major constituents including carvacrol, thymol, sabinene, trans- and cis-sabinene hydrate, germacrene D, β-caryophyllene, (Z)-β-ocimene, and (E)-β-ocimene. Carvacrol is recognized as the principal compound responsible for the biological activities attributed to the essential oil of *O. vulgare.* In Türkiye, *O. vulgare* essential oils were predominantly detected as the carvacrol chemotype, with carvacrol content reported as up to 85.4%. Thymol, linalool, γ-terpinene, and p-cymene compounds were also measured in *O. vulgare* essential oils derived from Türkiye, but their proportions are lower and vary depending on the region. [131–135]. There are studies in the literature demonstrating the strong antimicrobial, antioxidant, anti-inflammatory, and anti-aging activities of *O. vulgare* essential oil and its active constituent, carvacrol [127,128,136–139]. *O. vulgare* essential oil's carvacrol content was detected as 79.5% in a study. Then the free radical scavenging, lipid peroxidation inhibition, and inhibition of skin-aging-related enzymes, such as collagenase, elastase, and hyaluronidase activities, were evaluated. *O. vulgare* essential oil exhibited significantly high antioxidant activity and potent inhibition of collagenase (92.0% $\pm$ 9.7) and elastase (53.1% $\pm$ 13.3), suggesting its superior potential as a natural anti-aging agent. Considering that rosacea is characterized by microbial dysbiosis, oxidative stress, and inflammation, *O. vulgare* essential oil and carvacrol highlight a promising therapeutic potential in managing this chronic skin condition [136]. Chaftar et al. investigated the antimicrobial properties of nineteen essential oils, including *O. vulgare* essential oil (OEO), using a microdilution assay to determine minimum inhibitory concentrations (MICs). The study focused on bacterial and fungal strains commonly implicated in skin infections, such as *Staphylococcus epidermidis*, *Pseudomonas aeruginosa*, *Trichophyton mentagrophytes*, and *Trichophyton rubrum*. Chemical analysis revealed that OEO is predominantly composed of carvacrol (66.89%) and thymol (4.65%), which are largely responsible for its potent antibacterial and antifungal effects against Gram-positive (MIC $\leq$ 1.13 mg/mL) and Gram-negative (MIC $\leq$ 0.34 mg/mL) bacteria, as well as fungal species (MIC $\leq$ 1.80 mg/mL). Based on these findings, the authors suggested that OEO could be a promising candidate for dermatocosmetic applications. Given its antimicrobial activity against skin-associated pathogens, OEO may offer therapeutic potential for managing microbial imbalances observed in rosacea [137]. In a study by Avola et al., *O. vulgare* essential oil (OEO) demonstrated significant anti-inflammatory properties and promoted wound healing in in vitro human keratinocyte NCTC 2544 models. Specifically, the study employed a scratch assay to mimic epidermal injury, allowing the assessment of keratinocyte migration and proliferation as indicators of re-epithelialization. OEO treatment accelerated wound closure and enhanced cellular viability, suggesting its ability to support tissue repair mechanisms and restore skin barrier integrity [138]. In a study by Han et al., *O. vulgare* essential oil (which was high in carvacrol content) suppressed inflammatory biomarkers such as monocyte chemoattractant protein 1 (MCP-1), vascular cell adhesion molecule 1 (VCAM-1), intracellular cell adhesion molecule 1 (ICAM-1), interferon gamma-induced protein 10 (IP-10), interferon-inducible T-cell alpha chemoattractant (I-TAC), and monokine induced by gamma interferon (MIG).

Additionally, *O. vulgare* essential oil was shown to enhance epidermal barrier integrity and regulate immune responses in the skin, with inhibition of tissue remodeling biomarkers, namely collagen I, collagen III, epidermal growth factor receptor (EGFR), matrix metalloproteinase 1 (MMP-1), plasminogen activator inhibitor 1 (PAI-1), and tissue inhibitor of metalloproteinase (TIMP) 1 and 2. Given that rosacea pathogenesis involves chronic inflammation, dysregulated immune signaling, and impaired barrier function, these findings highlight the potential of *O. vulgare* essential oil as a complementary therapeutic agent for rosacea management [139]. Further preclinical and clinical studies are necessary to validate its efficacy and safety in patients with rosacea. Table 8 compiles the available experimental and clinical studies investigating the potential application of common oregano essential oil in rosacea management.

Table 8. An overview of experimental and clinical data highlighting the potential benefits of common oregano essential oil in the management of rosacea.

Type of Active Extract Tested	Type of Experiment Used to Prove Activity	Active Compounds Responsible	Active Dose/Regimen	Most Probable Molecular Mechanism	Improvement Related to Rosacea	Reference
O. vulgare essential oil	In vitro enzymatic assays (collagenase, elastase, hyaluronidase inhibition); antioxidant assays (DPPH radical scavenging, FRAP, ferric thiocyanate lipid peroxidation assay)	Carvacrol (major constituent, 79.5%), thymol, p-cymene, and γ-terpinene	Collagenase inhibition: 92.0 ± 9.7% at 67 μg/mL (IC_{50} = 35.1 ± 0.9 μg/mL); elastase inhibition: 53.1 ± 13.3% at 25 μg/mL (IC_{50} = 24.3 ± 0.5 μg/mL); hyaluronidase inhibition: 16.7 ± 0.3% at 4 μg/mL; DPPH IC_{50}: 1.8 ± 0.8 mg/mL	Antioxidant-mediated suppression of ROS; inhibition of matrix metalloproteinases (collagenase/MMPs and elastase), preventing extracellular matrix degradation; reduced lipid peroxidation limiting ROS-induced MMP-1 and MMP-3 upregulation	Potential attenuation of rosacea-associated erythema and inflammatory tissue damage through oxidative stress reduction; preservation of dermal collagen and elastin integrity may contribute to improved skin barrier function and reduced skin sensitivity; indirect mitigation of rosacea progression via anti-inflammatory and antioxidative pathways	[136]
O. vulgare essential oil	In vitro antimicrobial microdilution assays (96-well plates) against Gram-positive and Gram-negative bacteria and fungi (yeasts, molds, dermatophytes); MIC determination according to CLSI-adapted protocols	Carvacrol (66.89%), p-cymene (21.20%), and γ-terpinene	Bacteria: MIC ≈ 1.13 mg/mL (Gram-positive), MIC ≈ 0.34–1.13 mg/mL (Gram-negative); fungi: MIC ≈ 1.80 mg/mL (yeasts and molds), MIC ≈ 0.45 mg/mL (dermatophytes)	Disruption of microbial cytoplasmic membrane integrity via hydrophobic interaction of phenolic monoterpenes (carvacrol); increased membrane permeability, depolarization, and leakage of intracellular components	Potential reduction in rosacea-associated microbial burden (e.g., opportunistic skin bacteria and yeasts); indirect mitigation of inflammation and erythema by lowering microbe-induced immune activation; possible benefit in papulopustular rosacea through antimicrobial and barrier-supportive effects	[137]
O. vulgare essential oil	In vitro human keratinocyte (NCTC 2544) model; inflammatory stimulation with IFN-γ (200 U/mL) + histamine (10^{-4} M); scratch wound healing assay; ROS (H_2DCFDA), RT-PCR, Western blot, immunofluorescence	Carvacrol (35.95%), thymol (25.02%), p-cymene (21.54%), linalool (4.26%), and γ-terpinene	Non-cytotoxic and effective concentration: 25 μg/mL (72 h); reference comparator: indomethacin 10 μM	Inhibition of pro-inflammatory signaling via downregulation of ICAM-1, iNOS, and COX-2; reduction in oxidative stress (ROS, 8-OHdG); modulation of ECM remodeling through suppression of MMP-1 and MMP-12; promotion of keratinocyte migration and controlled proliferation (PCNA modulation)	Potential attenuation of rosacea-associated inflammation and erythema by reducing oxidative stress and inflammatory mediators; support of epidermal barrier repair and tissue remodeling; possible benefit in papulopustular and erythematotelangiectatic rosacea through improved keratinocyte homeostasis and wound-healing capacity	[138]
O. vulgare essential oil	In vitro human dermal fibroblast disease model (BioMAP HDF3CGF) mimicking chronic skin inflammation and fibrosis; protein biomarker analysis (ELISA, multiplex immunoassays), antiproliferation assays, genome-wide gene expression (microarray, IPA pathway analysis)	Carvacrol (major constituent)	Non-cytotoxic, biologically active concentration: 0.0037% (*v*/*v*); treatment duration: 24–72 h depending on endpoint	Broad suppression of inflammatory and immune-related signaling (MCP-1, VCAM-1, ICAM-1, IP-10, I-TAC, MIG); inhibition of tissue remodeling and ECM degradation pathways (collagen I/III, MMP-1, PAI-1, TIMP-1/2, EGFR); immunomodulation via reduced M-CSF; global downregulation of inflammation-, fibrosis-, and cancer-related gene networks	Potential attenuation of rosacea-associated chronic inflammation and immune activation; reduction in dermal matrix degradation, contributing to erythema persistence and tissue damage; possible benefit in inflammatory and papulopustular rosacea phenotypes through modulation of fibroblast-driven inflammatory signaling and tissue remodeling	[139]

4. Discussion

Based on the studies summarized above, the present review synthesizes available evidence on herbal extracts and oils traditionally used in Anatolian medicine and evaluates their potential relevance for the management of rosacea. Although the majority of the included studies do not directly target rosacea as a primary clinical endpoint, their findings provide important mechanistic and symptomatic insights that are highly relevant to the pathophysiology of this chronic inflammatory skin disorder. In particular, anti-inflammatory, antioxidant, anti-erythematous, antimicrobial, and anti-angiogenic activities frequently reported for these herbal agents align closely with key processes implicated in rosacea, including neurovascular dysregulation, innate immune activation, oxidative stress, and chronic inflammation. Across the reviewed literature, notable variability exists in study design, experimental models, and outcome measures. Clinical studies often focus on symptom relief, such as erythema, irritation, or skin barrier dysfunction, rather than disease modification, whereas in vitro and in vivo investigations tend to emphasize molecular mechanisms, including cytokine modulation, inhibition of inflammatory mediators, and antioxidative capacity. This heterogeneity complicates direct comparison between studies but simultaneously highlights the multifactorial nature of rosacea and the need for integrative therapeutic approaches.

A key emerging concept from the reviewed evidence is the potential benefit of combining different plant species or extracts to achieve synergistic effects. Rather than relying on a single active compound, combination formulations may simultaneously address inflammation, oxidative stress, microbial imbalance, and vascular alterations. Notably, a patented formulation developed for rosacea, pityriasis rosea, and any other skin barrier disorders (Application No: TP-2020/17641) exemplifies this approach, incorporating hydroglyceric or hydro-alcoholic extracts of *M. recutita* (standardized for apigenin), *G. glabra* (standardized for glycyrrhizic acid), and *Cistus creticus* L. (rich in polyphenols), together with bentonite clay in solution and massage preparations, as well as oil-based formulations containing *H. perforatum* and *C. officinalis* macerated oils combined with essential oils of *Mentha piperita* L., *Origanum onites* L., and *Lavandula angustifolia* Miller [140]. Despite these promising findings, several limitations and challenges must be acknowledged. A major gap in the literature is the limited number of well-designed, rosacea-specific clinical trials evaluating herbal products under standardized conditions. Variations in plant species, plant organs used, extraction methods, chemical composition, and dosing regimens hinder reproducibility and translational applicability. In addition, issues related to safety, long-term use, potential irritancy, and interactions with conventional pharmacological treatments remain insufficiently explored. These aspects are particularly important given the sensitive skin phenotype commonly observed in rosacea patients.

In addition to the herbal species discussed in detail in this review, several other plants traditionally used in Anatolian medicine have been reported to possess anti-inflammatory, wound-healing, and skin-soothing properties that may also be relevant to rosacea management. Species such as *Malva sylvestris* L., *Achillea millefolium* L., *Sideritis* spp., *Verbascum thapsus* L., and *Nigella sativa* L. have been widely employed in traditional remedies for inflammatory and irritated skin conditions [141–154]. Their reported activities, including modulation of inflammatory mediators, enhancement of wound repair, antioxidant effects, and support of skin barrier function, overlap with key pathophysiological mechanisms involved in rosacea. Similarly, aromatic and resin-producing plants such as *Thymus* spp., *Artemisia* spp., and *Pinus* spp. have demonstrated antimicrobial, anti-inflammatory, and antioxidant properties in various experimental studies [141,145,155–162]. Although direct clinical evidence linking these species specifically to rosacea remains limited, their traditional dermatological use and mechanistic relevance suggest that they may represent

promising candidates for future investigation. Inclusion of such plants in future pharmacognostic and clinical studies could contribute to a more comprehensive understanding of the therapeutic potential of Turkish medicinal flora and support the development of multi-component, synergistic herbal formulations tailored to inflammatory skin disorders.

5. Conclusions

Although multiple topical and oral agents, as well as laser therapy, are available for the treatment of rosacea, their limitations, frequent adverse effects, and high costs often result in early discontinuation, thereby increasing interest in plant-derived formulations among clinicians and patients. This review highlights that various herbal extracts and oils, historically employed in traditional Anatolian medicine and documented in the literature for their anti-inflammatory, antioxidant, anti-allergenic, analgesic, antimicrobial, antiangiogenic, and anti-erythematous properties, hold considerable potential for the management of rosacea. Most clinical studies focus on alleviating specific symptoms rather than rosacea itself, especially with their anti-inflammatory and antioxidant activities, highlighting that research on herbal extract/oil represents a pioneering effort in pharmacognosy aimed at developing safer and more effective therapies with improved patient compliance. In this context, the combined use of multiple plant species in well-designed formulations may offer synergistic therapeutic effects in inflammatory dermatoses such as rosacea. Such multi-component formulations highlight the potential of synergistic phytochemical interactions targeting inflammation, erythema, microbial imbalance, and skin barrier dysfunction. However, standardization, safety assessment, dose optimization, and clinical validation constitute critical aspects that should be carefully considered by researchers and developers involved in the formulation of herbal-based products.

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