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Therapeutic Potential of Essential Oils in Human Immune Responses and Inflammatory Pathologies: A Systematic Review

verfasst von | submitted by

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Abstract

Background: Natural products are increasingly gaining importance as complementary or alternative therapies. Because conventional medications can cause side effects or lose their efficacy over time, natural substances are investigated for their potential. Essential oils -volatile and lipophilic mixtures extracted from aromatic plants primarily through steam distillation- are moving into the medical focus. Recent studies show their diverse pharmacological properties, among their strong anti-inflammatory, antioxidant, and immunomodulatory capacities, making them potential candidates for adjuvant therapy in the management of immune system disorders.

Objective: To examine the potential of essential oils to exert anti-inflammatory or antioxidant effects and to modulate human immune responses in clinical settings.

Methods: A systematic review was conducted. An electronic search of PubMed, Scopus, and Google Scholar was performed to identify English-language clinical trials published between 2000 and May 2026.

Results: 32 studies met the predefined inclusion criteria and were analyzed. The aggregated data showed that essential oils had a positive impact on:

- Systemic Inflammation and Immune Protection: Reduction in systemic inflammatory markers (e.g., CRP) and oxidative stress. In oncological settings, specific EOs alleviated chemotherapy-induced immunosuppression (e.g., preserving leukocyte and neutrophil counts) and delayed radiation-induced mucositis.
- Local Infection and Tissue Integrity: Microbial bioburden and localized inflammation in periodontitis, acne, and cutaneous dermatophytosis were lessened, showing comparable outcomes to standard medical therapies in certain trials.
- Immune-related Hypersensitivities: Relief of symptoms and measurable improvements in pulmonary function in patients with allergic rhinitis and asthma.

Conclusion: Essential oils demonstrate a broad spectrum of biological activities, with focus on their antioxidant, anti-inflammatory, and immunomodulatory properties. While clinical trials indicate therapeutic potential for both systemic and localized immune-related pathologies, the current evidence is often limited by methodological weaknesses, such as small sample sizes and short intervention periods. Therefore rigorously blinded trials with longer timeframe, to observe any possible side effects and to get the whole pharmacological picture with enough participants are required, before reliable clinical guidelines with essential oils can be established.

Zusammenfassung

Hintergrund: Phytopharmaka gewinnen als komplementäre oder alternative Therapieformen zunehmend an Bedeutung. Da konventionelle Medikamente häufig mit Nebenwirkungen verbunden sind oder im Laufe der Zeit an Wirksamkeit verlieren können, werden natürliche Substanzen verstärkt auf ihr therapeutisches Potenzial untersucht. In den Fokus rücken dabei auch ätherische Öle, leicht flüchtige und lipophile Gemische, die primär durch Wasserdampfdestillation gewonnen werden. Aktuelle Studien belegen ihre antiinflammatorischen, antioxidativen und immunmodulatorischen Eigenschaften, was sie zu vielversprechenden Kandidaten für eine adjuvante Therapie bei Erkrankungen des Immunsystems macht.

Zielsetzung: Untersuchung des antiinflammatorischen, antioxidativen und immunmodulatorischen Potenzials ätherischer Öle.

Methodik: Es wurde ein systematisches Review durchgeführt. Hierfür erfolgte eine elektronische Literaturrecherche in den Datenbanken PubMed, Scopus und Google Scholar, um englischsprachige klinische Studien, die im Zeitraum zwischen 2000 und Mai 2026 veröffentlicht wurden, zu identifizieren.

Ergebnisse: Insgesamt erfüllten 32 Studien die Einschlusskriterien und wurden analysiert. Die Daten zeigten, dass ätherische Öle einen positiven Einfluss auf folgende Bereiche hatten:

- Systemische Entzündungen und Immunschutz: Reduktion systemischer Entzündungsmarker (z. B. CRP) und oxidativem Stress. Im onkologischen Setting milderten bestimmte ätherische Öle eine chemotherapie-induzierte Immunsuppression (z. B. durch den Erhalt der Leukozyten- und Neutrophilenzahlen) und verzögerten das Auftreten einer strahleninduzierten Mukositis.
- Lokale Infektionen und Gewebeintegrität: Die mikrobielle Belastung und lokalisierte Entzündungen bei Parodontitis, Akne und kutanen Dermatophytosen wurden verringert. In bestimmten Studien wurden Ergebnisse erzielt, die mit medizinischen Standardtherapien vergleichbar waren.
- Immunbedingte Hypersensitivitäten: Linderung der Symptome und messbare Verbesserungen der Lungenfunktion bei Patienten mit allergischer Rhinitis und Asthma.

Schlussfolgerung: Ätherische Öle besitzen vielfältige pharmakologische Eigenschaften. Obwohl die evaluierten klinischen Studien ein therapeutisches Potenzial sowohl für systemische als auch für lokalisierte immunbedingte Pathologien aufzeigen, ist die derzeitige Evidenzlage häufig durch methodische Schwächen wie kleine Stichprobengrößen und kurze Interventionszeiten limitiert. Bevor verlässliche klinische Leitlinien für den Einsatz ätherischer Öle etabliert werden können, sind daher methodisch hochwertige, verblindete Studien mit größeren Teilnehmerzahlen und längeren Untersuchungszeiträumen erforderlich, nicht zuletzt, um mögliche Nebenwirkungen zu beobachten und ein vollständiges pharmakologisches Bild zu erhalten.

Table of Contents

1 Introduction to Essential Oils

Essential oils (EO) are characterized by their strong fragrance. They are lipophilic and highly volatile and generally possess a lower density compared to water. These complex substances are made of up to several hundred individual substances. [BGA-Schweiz, 2011].

EOs are synthesized by aromatic plants and trees as secondary metabolites. They are found in a wide variety of plant organs, like flowers, leaves, stems, bark, roots, fruits, and seeds. They are stored in specialized structures such as secretory cells, oil ducts, epidermal cells, or glandular hairs (trichomes). In nature, plants use EOs to draw in pollinators to spread their seeds. Additionally, besides their antimicrobial impact, they protect the plant by deterring herbivores and facilitate complex allelopathic interactions with neighboring flora [BGA-Schweiz, 2011].

The main components are usually terpenes and terpenoids, with monoterpenes and sesquiterpenes -alongside their oxygenated derivatives- dominating. Together, these can account for 85 % or more of the EO [Miguel, 2010].
Other common substance groups include alcohols (such as phenols and sesquiterpenols), ketones, terpene aldehydes, esters, ethers, and oxides. Phenylpropanoids (e.g., allyl and propenyl phenols) are also important components. Many accompanying substances are often only present in trace amounts, but nevertheless contribute significantly to the overall organoleptic profile (scent and taste) as well as biological activity [BGA-Schweiz, 2011; Miguel, 2010].
Biosynthetically, the constituents follow different pathways:

- Terpenoids are produced via the mevalonate pathway or the mevalonate-independent deoxyxylulose phosphate pathway.
- Phenylpropanoids are synthesized via the shikimate pathway [Miguel, 2010].

According to the European Pharmacopoeia (11th Edition, Main Work 2023), an EO has to be gathered from a botanically defined herbal drug of suitable quality by steam distillation, dry distillation, or a mechanical process without heating. In practice, the following methods are used for the extraction of aromatic substances:

- **Steam distillation:** This is the most common and oldest method. It is carried out at relatively low temperature and low pressure so that the heat-sensitive EO retains its natural composition. The process separates the end product into two phases: the actual EO and the aromatic water (hydrosol).
- **Dry distillation:** The herbal drug is heated at high temperatures in a suitable apparatus without the addition of water or steam.
- **Expression (Cold pressing):** A mechanical process is mainly used for citrus fruits. The plant is crushed without heating.
- **CO_2 extraction (supercritical carbon dioxide):** Compressed carbon dioxide is used as a solvent. This process only uses a moderate temperature (about 30 °C). CO_2 extraction produces EOs without any solvent residues [BGA-Schweiz, 2011; European Pharmacopoeia Commission, 2023].

Reports showed that EOs have been therapeutically used since antiquity. Because of their high antioxidant potential, they protect the cells by scavenging free radicals, which are associated with chronic diseases such as cancer or immunodeficiency. In immune cells, inflammation leads to an oxidative burst, which produces reactive oxygen and nitrogen species. These serve to fend off germs, but can damage tissue if overproduced. EOs were found to have a regulatory effect here [Miguel, 2010].
Despite the well-documented positive effects, chemical variability, caused by climate, time of harvest, and extraction methods, make standardization of the preparations difficult. Since current evidence is also primarily based on in-vitro and ex-vivo models, well-founded clinical trials in humans are essential to understand the full therapeutic potential of these substances safely and reproducibly. For this reason, the present systematic review specifically focuses on the analysis and evaluation of previous human studies in order to systematically summarize the existing evidence on the clinical efficacy and safety of EOs in humans.

2 Material and Methods

2.1 Search Strategy

The literature search was conducted between January and May 2026 across PubMed, Scopus, and Google Scholar. To ensure a thorough overview, the search encompassed all relevant articles published from the year 2000 up to May 2026.
For PubMed, the search string combined Medical Subject Headings (MeSH) and Title/Abstract keywords: ("essential oil"[Title/Abstract] OR "essential oils"[Title/Abstract] OR "Oils, Volatile"[Mesh]) AND (inflammation[Title/Abstract] OR immunomodulation[Title/Abstract] OR "immune system"[Title/Abstract] OR anti-inflammatory[Title/Abstract] OR anti-viral[Title/Abstract] OR antiviral[Title/Abstract] OR anti-bacterial[Title/Abstract] OR antibacterial[Title/Abstract] OR anti-microbial[Title/Abstract] OR antimicrobial[Title/Abstract] OR antioxidant[Title/Abstract]). The unfiltered query resulted in 15,390 records. Using the database's built-in filters (Species: Human; Language: English; Article types: Clinical Study, Clinical Trial, Controlled Clinical Trial, Randomized Controlled Trial) the results were reduced to 114 records.
For Google Scholar, a Boolean title-restriction syntax was applied to minimize agricultural and pre-clinical articles: intitle:("essential oil" OR "volatile oil") AND (inflammation OR anti-inflammatory OR antioxidant OR immunomodulation OR antimicrobial OR antiviral OR anti-bacterial) AND (human OR clinical OR trial OR patients) AND (placebo OR control OR "standard therapy" OR RCT) -animal -"in vitro" -review -rats -chicken -mouse -harvest -fertilizer. After excluding patents and legal documents, the results showed approximately 2,090 records. Because Google Scholar does not have a bulk-export function, Harzing's Publish or Perish software [Harzing, 2007] was utilized to extract and export the search results.
For Scopus, the search string applied to titles and abstracts was: TITLE-ABS (("essential oil" OR "essential oils" OR "volatile oil" OR "volatile oils") AND (inflammation OR immunomodulation OR "immune system" OR anti-inflammatory OR anti-viral OR antiviral OR anti-bacterial OR antibacterial OR anti-microbial OR antimicrobial OR antioxidant) AND (human OR clinical OR trial OR placebo OR patient* OR volunteer*)) AND NOT TITLE-ABS (harvest OR fertilizer) AND PUBYEAR > 1999 AND PUBYEAR < 2027 AND (LIMIT-TO (DOCTYPE,"ar")) AND (LIMIT-TO (LANGUAGE,"English")). This initial query yielded 4,092 records. Limiting the results to relevant subject areas (Medicine; Pharmacology, Toxicology and Pharmaceutics; Immunology

and Microbiology; Biochemistry, Genetics and Molecular Biology) effectively reduced the yield to 50 records.
Additionally, a supplementary second search was conducted in PubMed using combinations of core keywords: *"essential oil" AND inflammation*, *"essential oil" AND immunomodulation*, *"essential oil" AND "immune system"*, *"essential oil" AND anti-inflammatory*, *"essential oil" AND "C-reactive protein"*, *"essential oil" AND antiviral*, *"essential oil" AND antibacterial*, and *"essential oil" AND antimicrobial*.
Initial screening of titles and abstracts was performed directly within the respective databases. Subsequently, the selected citations were imported into the Rayyan web application [Rayyan Systems Inc., 2016] exclusively for data management and deduplication. Exact and partial duplicates among the combined results were identified using Rayyan's automated function.

2.2 Selection Criteria

Titles and abstracts of the retrieved articles were initially screened according to the PICO (Population, Intervention, Comparison, Outcome) criteria outlined in Table 1. Eligibility was restricted to original studies published in English reporting data involving human subjects. Purely pre-clinical investigations (standalone in-vitro assays or in-vivo animal models) and review articles were excluded. Articles evaluating broader botanical preparations (e.g., fixed plant oils, extracts, or powders) were eligible only if the authors attributed the observed immunomodulatory effects to the EO fraction or its standardized volatile bioactives.
Although *Nigella sativa* oil is technically classified as a fixed carrier oil due to its high content of polyunsaturated fatty acids, it was explicitly included in this systematic review. The rationale lies in its potent volatile fraction, primarily the monoterpene ketone thymoquinone. In accordance with the predefined inclusion criteria, the selected clinical trials utilized extracts that were either standardized specifically to this EO constituent or attributed the observed pharmacological outcomes directly to it. In this context, the non-volatile matrix acts primarily as a biogenic carrier, while the volatile monoterpene fraction functions as the primary pharmacological driver of the observed immunomodulatory and metabolic effects.
Commercially formulated products, such as Listerine mouthwash, were excluded from this review.

Table 1: PICO (Population, Intervention, Comparison, Outcome) criteria for study inclusion.

Parameter	**Inclusion Criteria**
Population	Studies performed in humans
Intervention	Treatment with Essential Oils and Essential-Oil-Bearing Botanicals
Comparison	Placebo or standard therapy
Outcome	Anti-inflammatory, antioxidant, or immunomodulatory effects

2.3 Data Extraction

The extracted data were organized according to distinct descriptors and summarized in the following tables:

- **Table 2:** Lists the major phytochemical constituents described in the included studies.
- **Table 3:** Summarizes baseline study characteristics, including mentioned plant, main active components, and primary/secondary endpoints.
- **Table 4:** Details the study designs, sample sizes, inclusion criteria, and time frames.
- **Table 5:** Outlines the application form, drop-out rates, study arms, and statistically significant results.
- **Table 6:** Presents the methodological quality assessment of the trials using the Jadad score.

2.3.1 Methodological Quality

The Jadad scale, developed in 1996, is an established and widely recognized tool for assessing the methodological quality of randomized controlled trials. The scoring system evaluates randomization, blinding, and patient dropouts, which directly affect a study's reliability [De Cassai et al., 2023].

Using this system, the methodological quality of the 32 analyzed studies was evaluated in detail (as shown in Table 6). The assessment is based on five distinct yes/no questions (scored 0 = No, 1 = Yes):

1. Was the study described as randomized?
2. Was the method of randomization appropriate?
3. Was the study described as blinded?
4. Was the method of blinding appropriate?
5. Was there a description of withdrawals and drop-outs?

This results in a possible score ranging from zero to five points. In general, studies with a score of 3 or higher are considered to be of high methodological quality. Scores below 3 indicate weaknesses in the study design and are associated with a higher risk of bias. [Jadad et al., 1996; De Cassai et al., 2023]. This systematic scoring provides a reliable framework for objectively assessing the impact of reviewed studies.

2.3.2 General Assessment of Study Quality

Overall, the included studies exhibit a moderate to high methodological quality:

- **Very high methodological quality (Score 5):** These studies met all five evaluation criteria, providing a reliable evidence base with a low risk of bias [Beheshti Roy et al., 2014; Botelho et al., 2009; Duijker et al., 2015; Eshwar et al., 2016; Majeed et al., 2024; Mohan et al., 2023; Morovati et al., 2019; Newman et al., 2022; Salem et al., 2023; Tavakoli-Rouzbehani et al., 2022].

- **Good methodological quality (Scores 3–4):** These studies had a solid fundamental design, but lost points in one or two categories. In most cases, this was due to the lack of an explicit description of appropriate randomization or blinding methods (Questions 2 and 4). A substantial number of studies achieved a score of 3 [Amerikanou et al., 2023; Asih et al., 2021; Dryden et al., 2004; Maddocks-Jennings et al.,

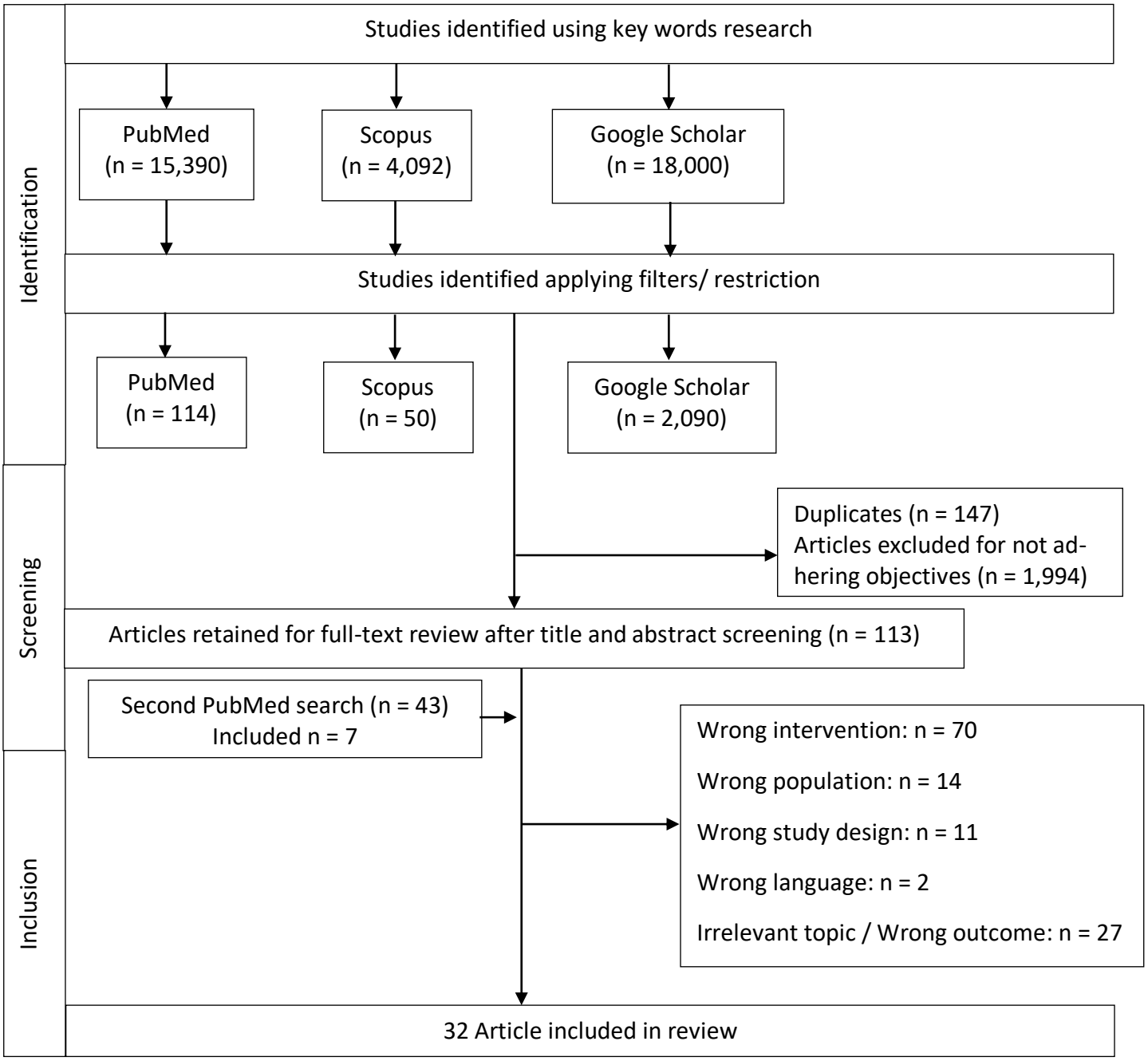
2009; Nasirzadeh et al., 2023; Panahi et al., 2014; Saeidi et al., 2024; Taalab et al., 2021] or a score of 4 [Alavinezhad et al., 2018; Amanlou et al., 2007; Ghorani et al., 2021; Joksimovic et al., 2012; Zhuang et al., 2009].

- **Low methodological quality (Scores 1–2):** Some included trials achieved low scores, indicating methodological vulnerabilities. Studies scoring 2 points include several trials [Casetti et al., 2012; Hi and Endang (2020); Mazzarello et al., 2020; Seol et al., 2016], while others scored only 1 point [Ahirwar et al., 2018; Ghitea et al., 2021; Khalil et al., 2004; Pearce et al., 2005; Sallam, 2009]. The results of these specific trials should be interpreted with caution due to methodological limitations, such as a lack of double-blinding or insufficient randomization protocols.

3 Study Selection

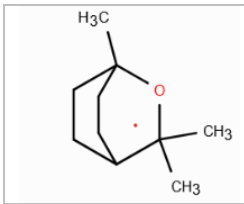
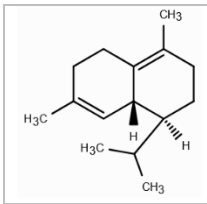
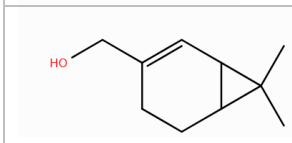
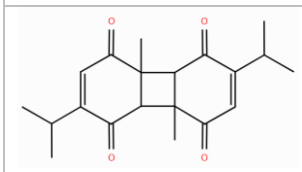
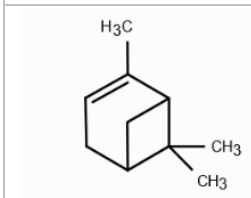
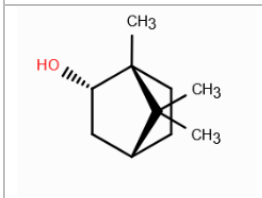
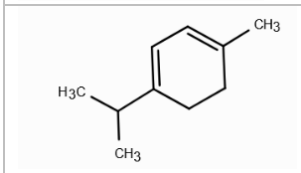
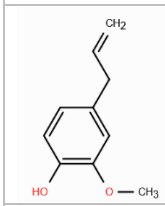
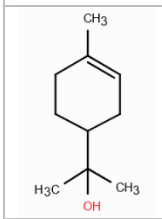
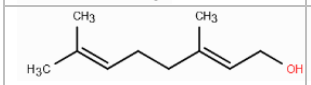
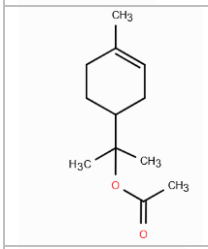
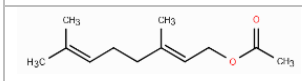
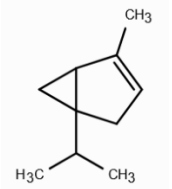
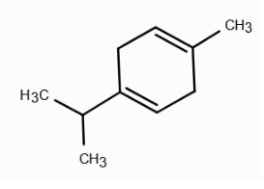
32 relevant articles were identified and included in this review. The complete selection process is illustrated in Figure 1, conforming to the PRISMA flow diagram guidelines.

Figure 1: PRISMA flow diagram



3.1 Phytochemical Constituents

Table 2: Major phytochemical constituents identified in the plant-derived products included in this review [chemical structures retrieved from Royal Society of Chemistry, 2026].

	1,8-cineole		*δ*-cadinene
	2-caren-10-al		dithymoquinone
	*α*-pinene		*endo*-borneol
	*α*-terpinene		eugenol
	*α*-terpineol		geraniol
	*α*-terpinyl acetate		geranyl acetate
	*α*-thujene		*γ*-terpinene

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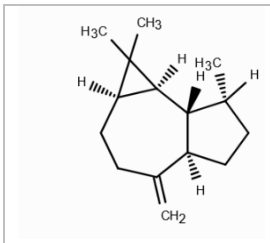
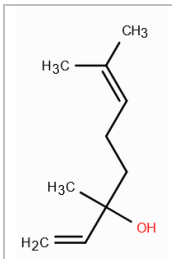
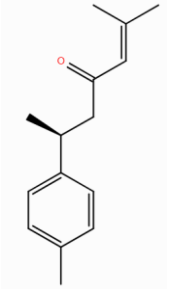
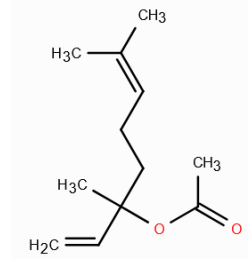
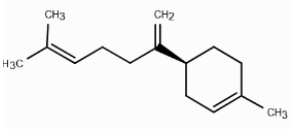
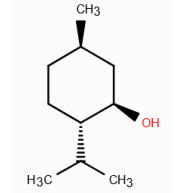
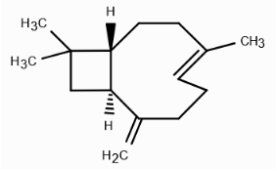
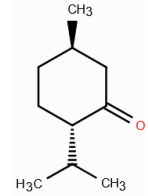
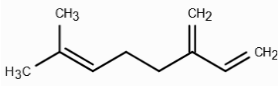
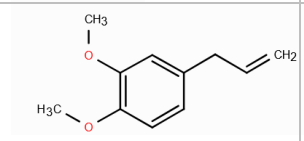
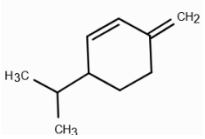
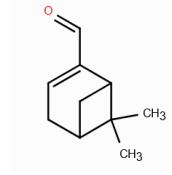
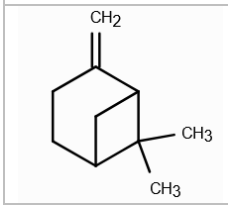
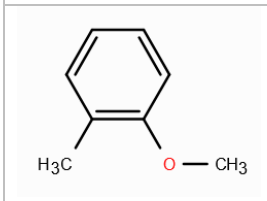
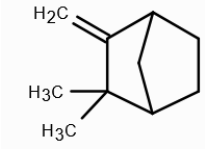
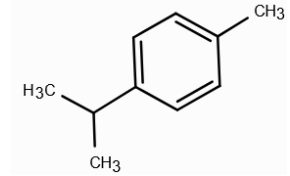
	aromadendrene		linalool
	*ar*-turmerone		linalyl acetate
	*β*-bisabolene		menthol
	*β*-caryophyllene		menthone
	*β*-myrcene		methyleugenol
	*β*-phellandrene		myrtenal
	*β*-pinene		*o*-methylanisole
	camphene		*p*-cymene

Table 2 continued

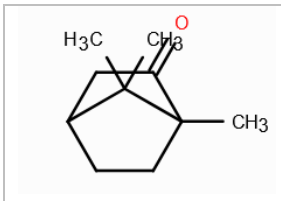
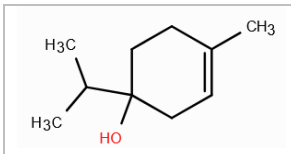
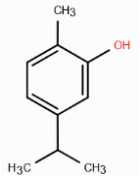
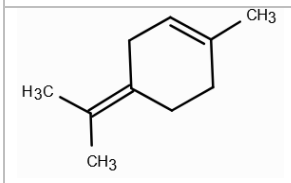
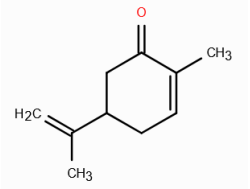
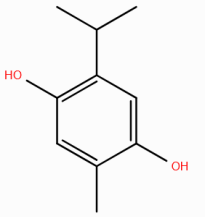
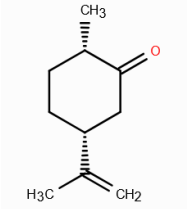
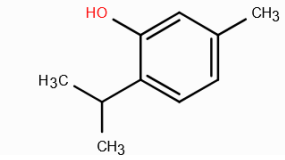
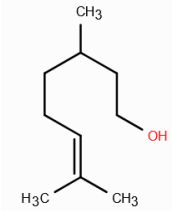
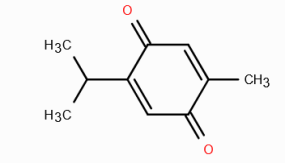
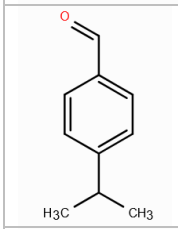
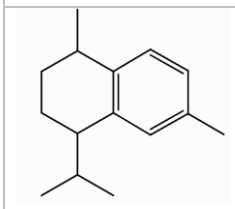
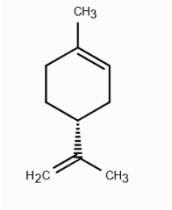
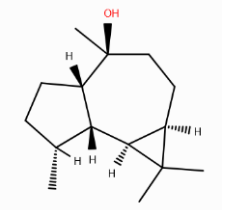
	camphor		terpinen-4-ol
	carvacrol		terpinolene
	carvone		thymohydroquinone
	*cis*-dihydrocarvone		thymol
	citronellol		thymoquinone
	cuminaldehyde		*trans*-calamenene
	*d*-limonene		viridiflorol

Table 3: Summary of study data: Author's name/year of publication, plant, main active components, primary endpoints, and secondary endpoints

Reference	**Plant**	**Major Active Constituents**	**Primary Endpoints**	**Secondary Endpoints**
Eshwar et al. (2016)	*Anethum Graveolens*	d-carvone, d-limonene	plaque levels, gingivitis severity	
Saeidi et al. (2024)	*Berberis integerrima* Bunge, *Mentha spicata* L.	carvone (80.5%), dl-limonene (12.3%), menthol (1.5%), menthone (0.9%)	number of lesions, modified global acne grading scale score	number of completely treated lesions
Casetti et al. (2012)	*Coriandrum sativum* L.	linalool (75.9%), camphor (5.2%), *α*-pinene (4.2%), limonene (2.2%), geranyl acetate (2.1%), *p*-cymene (1.4%), geraniol (1.1%), *α*-terpineol (0.6%)	1) in-vitro: evaluation of the antibacterial activity (MIC, MBC) against bacteria with dermatological relevance (e.g., *S. pyogenes, S. aureus*, MRSA) 2) in-vivo: assessment of skin tolerance and potential for skin irritation	comparison of antimicrobial efficacy against standard reference antibiotics
Duijker et al. (2015)	*Coridothymus capitatus* L., *Origanum dictamnus* L., *Salvia fruticosa* Mill., *Salvia pomifera* L.		severity and duration of symptoms of upper respiratory tract infection (Wisconsin Upper Respiratory System Survey)	
Morovati et al. (2019)	*Cuminum cyminum* L.	cuminaldehyde, p-cymene, *β*-pinene, *β*-phellandrene, cis-dihydrocarvone, myrtenal, 2-caren-10-al	MDA, SOD, TAC, CAT, GSH-Px, CRP, TNF-α	daily energy and dietary nutrient intakes

Table 3 continued

Zhuang et al. (2009)	*Ganoderma lucidum*, *Codonopsis pilosula*, *Angelica sinensis*	citronellol	leukocytes, neutrophils, lymphocytes, CD3, CD4, CD8, NK cells, B cells, red blood cells, hemoglobin, hematocrit, platelets	
Asih et al. (2021)	*Mentha piperita, Lavandula angustifolia, Curcuma longa*	menthol, linalool, *ar*-turmerone	pruritus scores (Visual Analog Scale)	
Maddocks-Jennings et al. (2009)	*Leptospermum scoparium, Kunzea ericoides*	*trans*-calamenene, viridiflorol	development of radiation-induced mucositis, pain, effects on nutritional status (including weight changes)	mood, coping
Botelho et al. (2009)	*Lippia sidoides*	thymol (56.67%), carvacrol (16.73%), p-cymene (7.13%), 1.8-cineol (2.39%), terpinene (1.42%)	colony count of *Streptococcus mutans* from stimulated saliva and periodontal indices (PI, GI, and Gingival Bleeding Index)	adverse events
Beheshti Roy et al. (2014)	*Melaleuca Alternifolia*	terpinen-4-ol (41.1%), *γ*-terpinene (21.0%), *α*-terpinene (11.4%), 1,8-cineole (4.7%), *α*-terpineol (3.1%), *p*-cymene (2.6%), terpinolene (2.4%), *α*-pinene (1.9%), aromadendrene (1.7%), *δ*-cadinene (1.0%), limonene (0.9%)	extent of itching, erythema, scaling, greasy crusts	patient satisfaction, occurrence of side effects
Dryden et al. (2004)	*Melaleuca Alternifolia*	terpinen-4-ol	clearance of MRSA colonization	comparison of the effectiveness

Table 3 continued

Joksimovic et al. (2012)	*Melaleuca Alternifolia*		anal pain intensity, pain during defecation, bleeding, pruritus, irritation, recorded by patients and investigators using a visual analogue scale (VAS 0-10); safety, tolerability	assessment of the disease
Khalil et al. (2004)	*Melaleuca Alternifolia*	terpinen-4-ol (42%), *α*-terpineol (3%), 1,8-cineole (2%)	1) human study: regulation of histamine-induced wheal volume and flare area 2) rodent study: changes in microvascular blood flow (vasodilation) and protein extravasation (edema) in rat skin blisters	Characterization of the specific mechanisms of action (pre-terminal vs. post-terminal events) pre- and post-sensory nerve terminal events
Pearce et al. (2005)	*Melaleuca Alternifolia*	terpinen-4-ol, 1,8-cineole	mean erythema index and flare area (cm^2) of the nickel-induced contact hypersensitivity reactions	regulatory effects of tea tree oil on the proliferative response to nickel or polyclonal mitogens by peripheral blood mononuclear cells
Taalab et al. (2021)	*Melaleuca Alternifolia*	1,8-cineole, terpinen-4-ol	pocket probing depth PPD, clinical attachment loss CAL, gingival index GI, bleeding on probing BOP, matrix metalloproteinase-8 MMP-8	
Mazzarello et al. (2020)	*Myrtus communis* L., *Origanum vulgare*		comedones, papules, pustules, Total Lesion Count, Acne Severity Index, skin sebum, pH, Transepidermal Water Loss, Erythema Index	
Hi and Endang (2020)	*Nigella sativa*	thymoquinone	levels of Nuclear factor erythroid 2-related factor 2	Clinical conditions (BMI, blood pressure, blood glucose, triglyceride, total cholesterol, HDL)
Majeed et al. (2024)	*Nigella sativa*	thymoquinone, thymohydroquinone, dithymoquinone, thymol, carvacrol	change in Total Nasal Symptom Score (TNS)	Total Ocular Symptom Score, IgE, Patient Global Impression of Change

Table 3 continued

Mohan et al. (2023)	*Nigella sativa*	thymoquinone, carvacrol	sleep quality: Pittsburgh Sleep Quality Index (PSQI), stress: Perceived Stress Scale-14 (PSS-14)	salivary cortisol, salivary melatonin, plasma Orexin A, IgG and IgM, CD4+ and CD8+ absolute counts, differential WBC count, IL-1β, IL-2, IL-10
Salem et al. (2023)	*Nigella sativa*	thymoquinone	heart rate, systolic and diastolic blood pressure, mean arterial pressure, lymphocyte absolute count, CD3+ T-lymphocytes, CD4+ T-helper cells, CD8+ T-suppressor cells, CD19+ B-lymphocytes, NK cells, CD4+/CD8+ ratio, IgG, IgM, IL-1β, IL-4, IL-6, IL-10, TNF, Gene expression: IFN-γ, NF-κB, TNF-α, IL-1β, IL-13, IL-8, IL-6	
Sallam (2009)	*Nigella sativa*	thymoquinone	clinical: Disease Activity Score, Ritchie Articular Index, morning stiffness in minutes, erythrocyte sedimentation rate, Visual Analogue Scale of pain, hemoglobin, WBC count, platelets; experimental: paw edema, alanine aminotransferase, aspartate aminotransferase	
Tavakoli-Rouzbehani et al. (2022)	*Nigella sativa*	thymoquinone	serum levels of adhesion molecules, oxidative markers, atherogenic parameters	lipid profiles (TC/HDL-C, LDL-C/HDL-C, non-HDL-C), anthropometric parameters (weight, BMI, waist circumference), physical activity, dietary intakes
Ahirwar et al. (2018)	*Ocimum sanctum Linn.*	eugenol, carvacrol, methyl-eugenol	Evaluate and compare antimicrobial efficacy to a triple antibiotic paste (reduction in CFUs)	

Table 3 continued

Ghitea et al. (2021)	*Origanum vulgare* L.	carvacrol (29.22%), linalool (11.18%), thymol (3.62%), *endo*-borneol (3.39%), terpinen-4-ol (2.89%), *β*-bisabolene (2.65%)	antibacterial efficacy, impact on the phase angle (a bioimpedance marker for cellular health and function)	Presence of gastrointestinal side effects
Amerikanou et al. (2023)	*Pistacia lentiscus*	*α*-pinene (82.5%), *β*-myrcene (10.5%), *β*-pinene (2.52%), limonene (0.67%), *β*-caryophyllene (0.55%), camphene (0.41%), *α*-thujene (0.77%), *o*-methylanisole (0.22%)	changes in blood lipids: triglycerides, total cholesterol and LDL, and in insulin sensitivity (glucose, insulin)	changes in inflammatory and OS status indices (CRP, myeloperoxidase, IL-6)
Amanlou et al. (2007)	*Satureja khuzistanica* Jamzad	carvacrol (92.5%), thymol (1.1%), *p*-cymene (0.9%), eugenol (0.8%)	pain elimination, complete healing of lesions	
Panahi et al. (2014)	*Syzygium aromaticum, Lavandula angustifolia, Geranium robertianum*	eugenol, linalool, geraniol, citronellol	alleviation of acute external otitis symptoms, reduction in the burden of infection determined by ear discharge cultures	pain severity recorded using a Visual Analogue Scale
Nasirzadeh et al. (2023)	*Zataria Multiflora*	carvacrol (46.56%), thymol (40.67%)	inflammation, itching, scaling, size of cutaneous lesions, patient and dermatologist approval	
Alavinezhad et al. (2018)		carvacrol	pulmonary function tests (FVC, MMEF, PEF, MEF75, MEF50, MEF25), respiratory symptoms, CRP, total WBC, neutrophils, lymphocytes, monocytes, eosinophils, basophils, RBC, Hb, Hct, MCV, MCH, MCHC, platelets	

Table 3 continued

Ghorani et al. (2021)		carvacrol	respiratory symptoms (night wheeze, night cough, chest wheeze); pulmonary function tests (Peak expiratory flow, forced vital capacity, maximum mid-expiratory flow); Oxidative stress markers (Nitrite, MDA, SOD, thiol, CAT); cytokines (IL-4, IL-10, IFN-γ, peripheral blood mononuclear cells)	
Seol et al. (2016)		linalool	1,1-Diphenyl-2-picrylhydrazyl (DPPH) radical scav-enging activity, systolic blood pressure, diastolic blood pressure, pulse rate	
Newman et al. (2022)		menthol, 1,8-cineol, methyl salicylate, thymol	PI	GI, BOP, PPD, changes in the composition of the su-pragingival microbiome, safety assessments

Table 4: Summary of study design, sample size, inclusion criteria, and time frame

Reference	**Design**	**n**	**Eligibility criteria for participants**	**time frame**
Eshwar et al. (2016)	randomized, double-blind, parallel-group clinical trial	60	Dental students (18 - 25 y) with good general health, minimum of 20 erupted teeth, baseline PI > 1.5, baseline GI > 1.0	15 days
Saeidi et al. (2024)	randomized controlled clinical trial	75	Patients (≥ 12 y) having mild to moderate acne vulgaris on the face	4 weeks
Casetti et al. (2012)	in-vitro microbiological evaluation and a prospective, randomized, placebo-controlled double-blind study	40	Patients (≥ 18 y), healthy, non-smoking	48 hours
Duijker et al. (2015)	randomized, double-blind, controlled trial	108	Patients (≥ 18 y) with symptoms of upper respiratory tract infection	7 days
Morovati et al. (2019)	randomized, triple blind, placebo- controlled clinical trial	56	Patients (18 – 60 y) with increased waist circumference, elevated blood pressure, triglycerides and/or reduced high-density lipoprotein, elevated fasting glucose	8 weeks
Zhuang et al. (2009)	randomized, double-blind, placebo-controlled clinical trial	105	Cancer patients, who were undergoing chemotherapy and/or radiotherapy	6 weeks
Asih et al. (2021)	randomized single-blind, clinical trial	60	Pregnant women at 25 – 38 weeks of gestation, diagnosed with level I and II pruritus	2 weeks

Table 4 continued

Maddocks-Jennings et al. (2009)	randomized, placebo-controlled feasibility study	21	Patients (> 18 y) undergoing non-palliative radiotherapy to the head and neck area for at least four weeks	2 days before/on the day of radiotherapy until a week after
Botelho et al. (2009)	randomized, controlled, double-blind clinical trial	55	Patients (18 – 69 years) with a minimum of 10 natural teeth, a mean PI of at least 1.05, and a mean GI of at least 1.0	30 days (7 days treatment)
Beheshti Roy et al. (2014)	randomized, double-blind, placebo-controlled clinical trial	54	Patients (18 – 45 y) with mild-to-moderate facial seborrheic dermatitis	4 weeks
Dryden et al. (2004)	randomized, controlled trial	236	Hospitalized patients with confirmed MRSA colonization	5 days
Joksimovic et al. (2012)	double-blind, placebo-controlled clinical	36	Patients (18 y) with haemorrhoid (I - III)	2 weeks

Table 4 continued

Khalil et al. (2004)	complementary human and rodent studies	40	Patients, healthy	1 hour
Pearce et al. (2005)	prospective, controlled clinical study with intra-individual comparison	18	Patients (19 - 67 y) with nickel hypersensitivity	7 days
Taalab et al. (2021)	randomized, controlled clinical trial	30	Patients (25 – 50 y) with stage 2 periodontitis	6 months

Table 4 continued

Mazzarello et al. (2020)	comparative, randomized, single-blind trial	60	Patients (14 – 34 years) in good health with no topical/systemic therapies for at least 3 months; presenting with mild-moderate facial acne (maximum of 20–50 papules, pustules, and comedones); scarring in the erythematous phase; absence of nodulocystic lesions	30 days
Hi and Endang (2020)	analytical observational study with a cohort design	62	Patients (> 18 y); possessing at least 3 of 5 metabolic syndrome criteria	20 days
Majeed et al. (2024)	randomized, double-blind, placebo-controlled study	65	Males (18 – 60 y), diagnosis of seasonal allergic rhinitis, at least two symptoms (sneezing, runny nose, nasal congestion, itching) for more than 1 hour per day	15 days
Mohan et al. (2023)	randomized, double-blinded, placebo-controlled clinical trial	72	Patients (25 - 65 y), healthy, PSQI scores ≥ 5; PSS score 14 to 26; body weight ≥ 50 kg	90 days
Salem et al. (2023)	randomized, double-blinded, placebo-controlled clinical trial	76	Patients (18 – 25 y) with a BMI between 18.5 and 29.9 kg/m2, healthy	4 weeks
Sallam (2009)	in-vivo experimental animal study combined with a sequential, placebo-controlled clinical trial	60	Patients with rheumatoid arthritis, combined standard therapy of methotrexate, hydroxychloroquine and folic acid	4 weeks

Table 4 continued

Tavakoli-Rouzbehani et al. (2022)	randomized, double-blind, placebo-controlled clinical trial	49	Patients (35 – 65 y) undergoing angiography with a minimum of 50 % stenosis in at least one of the main coronary arteries	8 weeks
Ahirwar et al. (2018)	randomized clinical trial	40	Patients (4 - 9 y); teeth with evident clinical signs of furcal abscess, periapical abscess or draining sinus; periapical changes visible on a radiograph; at least 2 / 3rd of the root length available	3 days
Ghitea et al. (2021)	comparative observational/clinical study	106	Patients with metabolic syndrome with minor uncomplicated infections	10 days
Amerikanou et al. (2023)	randomized controlled clinical trial	94	Patients (18 – 75 y) with abdominal obesity (waist circumference > 94 cm for males and > 80 cm for females), and the presence of at least one metabolic abnormality: 1. triglyceride level ≥ 150 mg/dL or HDL cholesterol ≤ 40 mg/dL in men and ≤ 50 mg/dL in women, 2. increased blood pressure ≥ 130/85 mm Hg, 3. elevated fasting blood sugar ≥ 100 mg/dL	3 months
Amanlou et al. (2007)	randomized, double-blind clinical trial	60	Patients (10 - 64 y) with recurrent aphthous stomatitis, currently suffering from ulceration (minor aphthae) on oral mucosa	1 week
Panahi et al. (2014)	randomized, comparative, non-inferiority clinical trial	80	Patients (18 – 60 y) with initial acute external otitis symptoms	7 days
Nasirzadeh et al. (2023)	randomized, double-blind placebo-controlled, clinical trial	80	volunteers (> 10 years) who suffered from mild to moderate cutaneous dermatophytosis (except for tinea ungium and tinea capitis); no previous antifungals application	4 weeks

Table 4 continued

Alavinezhad et al. (2018)	randomized, double-blind, placebo-controlled, clinical trial	23	Patients (20 - 70 y) with moderate to severe asthma (diagnosed based on GINA guidelines), two or more specific symptoms, having an FEV 1 and PEF of less than 80 %	2 months
Ghorani et al. (2021)	randomized, placebo-controlled, double-blind, clinical trial	33	Patients (20 - 70 y), diagnosed with mild-to-severe asthma according to the Global Initiative for Asthma guideline, exhibiting respiratory symptoms, showing reduced pulmonary function tests	2 months
Seol et al. (2016)	double-blind, placebo-controlled study	37	Patients with no underlying disease, patients with Carpal tunnel syndrome (CTS) diagnosed by electrodiagnostic tests	10 minutes
Newman et al. (2022)	randomized, controlled, double-blind clinical trial	118	Healthy patients (18 - 60 years), at least 20 gradable teeth, having 10 or more bleeding sites at baseline	12 weeks

Table 5: Summary of study data: Author's name/year, application form, drop-outs, study arms, and the statistically significant results

Reference	Application	Dropout	Study Arms	Results
Eshwar et al. (2016)	Mouthrins	0	1) 0.5 % dill seed oil 2) Control: 0.12 % chlorhexidine	reduction: PI, GI from baseline in both groups ($p < 0.05$) or 15-day intervals ($p > 0.05$)
Saeidi et al. (2024)	topical solution (twice a day)	15	1) 5 % Berberis root dried extract and 1 % spearmint EO 2) Control: 1 % clindamycin	reduced the number of lesions ($p < 0.001$) and mGAGS ($p < 0.001$), no significant difference between intervention and control group
Casetti et al. (2012)	occlusive patch test	no mention	1) 0.5 % lotion 2) 1 % lotion 3) 0.5 % cream 4) 1 % cream 5) Placebo lotion/ cream	agar dilution test: pronounced growth inhibition of most of the bacteria strains tested *S. pyogenes* (MIC 0.04 % v/v); *S. viridans* (MIC 0.08 %v/v))
Duijker et al. (2015)	soft-gel capsules (two times daily)	3	1) EO (0.5 ml) 2) Control	CRP levels were normalized within the intervention group ($p = 0.016$)
Morovati et al.	soft gel	12	1) EO (75 mg)	SOD ($p = 0.001$), TAC ($p = 0.002$), MDA ($p = 0.01$) concentration
Table 5 continued				
Zhuang et al. (2009)	Capsules	34	1) citronellol powder (273.6 mg), Angelica extract (64.5 mg), Codonopsis Pilosulae Radix extract (27.1 mg), Ganoderma extract (3.0 mg) 2) Control	intervention: reduced depletion of leukocytes (14.2 % compared with 28.2 %), neutrophils (11.0 % compared with 29.1 %); reduction only in placebo: hematocrit, platelet concentration, mean percentage of CD4 lymphocytes, NK cells
Asih et al. (2021)	Oil	3	1) virgin coconut oil mixed at a ratio of 1 % peppermint, 1 % lavender and 1 % turmeric 2) Control: virgin coconut oil	severity of pruritus (VAS score) decreased from baseline mean of 62.7 mm to 22.4 mm ($p < 0.001$); pruritus reduction in intervention group higher (61.08 % versus 12.41 %, $p < 0.05$)

Table 5 continued

Maddocks-Jennings et al. (2009)	gargle solution	2	1) 2 drops of a 1:1 mix of manuka and kanuka oil diluted in water 2) Placebo: sterile water 3) Control: without a gargle solution	delayed mucositis: first reaction at a mean radiation dose of 3120 cGy, whereas placebo group at 1450 cGy, control group at 2163 cGy ($p = 0.05$)
Botelho et al. (2009)	mouthrinse (twice daily)	16	1) 1 % EO 2) Control: 0.12 % chlorhexidine	both groups: decrease in mean GI, PI, and Gingival Bleeding Index scores at 7 and 30 days compared to baseline ($p < 0.001$); reduction in the salivary colony count of *S. mutans* in both groups compared to baseline ($p < 0.05$)
Beheshti Roy et al. (2014)	gel (three times a day)	12	1) 5 % tea tree oil gel 2) Control	decrease in scores for itching, erythema, scaling, and greasy crusts compared to the placebo group ($p < 0.05$), patient satisfaction scores reported a "total cure" in 91% ($n = 21$) by 4 weeks
Dryden et al. (2004)	nasal ointment (three times a day), body wash and cream (at least once daily)	12	1) 10% tea tree cream, 5 % tea tree body wash, 10 % tea tree cream 2) Control: mupirocin 2 % nasal ointment, chlorhexidine gluconate 4 % soap, silver sulfadiazine 1 % cream	no significant difference in clearance of MRSA carriage except in the nostrils
Joksimovic et al. (2012)	topical gel	no mention	1) hyaluronic acid, tea tree oil, methyl-sulfonyl-methane 2) placebo	pain during evacuation, pruritus, irritation and visible bleeding ($p < 0.001$), for pain ($p < 0.05$), patient evaluation ($p < 0.001$)

Table 5 continued

Khalil et al. (2004)	topical (10 and 20 min after histamine injection)	no mention	1) tea tree oil 2) terpinen-4-ol 3) 1,8-cineole 4) α-terpineol 5) Control: Histamine injection without tea tree oil/component application	human study: tea tree oil and terpinen-4-ol reduced histamine-induced wheal and flare response, terpinen-4-ol reduced the histamine-induced erythema index; rodent Study: 1,8-cineole reduced microvascular blood flow following sensory nerve stimulation, terpinen-4-ol reduced substance P-induced protein extravasation
Pearce et al. (2005)	topical application in-vivo; in-vitro	no mention	1) tea tree oil (100 %) 2) 5 % tea tree oil lotion 3) placebo lotion 4) 100 % macadamia oil	tea tree oil (100 %): reduced mean flare area, erythematous response and nickel-induced proliferation of peripheral blood mononuclear cells
Taalab et al. (2021)	Gel	0	1) scaling, root planing and 5 % tea tree oil 2) Control: scaling and root planing alone	CAL at six months: mean CAL ($p = 0.004$), mean percentage reduction in CAL ($p = 0.003$); GI at both three and six months: mean GI ($p = 0.005$), mean percentage reduction in GI ($p = 0.029$, $p = 0.001$); BOP at six months: mean BOP ($p = 0.002$), mean percentage reduction in BOP ($p = 0.001$); MMP-8 values at six months: decrease ($p = 0.005$), mean percentage reduction in MMP-8 levels at three and six months ($p = 0.003$, $p < 0.001$)
Mazzarello et al. (2020)	Cream	0	1) 3.74 % of *M. communis* EO, 0.1% *O. vulgare* EO, 0.025 % tretinoin 2) Control: 1 % clindamycin, 0.025% tretinoin (Acnatac gel)	Transepidermal Water Loss: worsened in both groups; intervention improved papular erythema starting at 15 days compared to control ($p = 0.0329$): erythema on healthy skin increased in control ($p = 0.0017$ at 30 days); both treatments improved pustels, Acne Severity Index, Total Lesion Count at 15 and 30 days compared to baseline
Hi and Endang (2020)	soft capsules	0	1) black seed oil (3mL/day) 2) Placebo	no statistically significant results

Table 5 continued

Majeed et al. (2024)	capsule	0	1) 5% thymoquinone and 2.5 mg piperine (250 mg) 2) Control	Change in Total Nasal Symptom Score, Total Ocular Symptom Score, Patient Global Impression of Change
Mohan et al. (2023)	soft gel capsule	10	1) black cumin oil extract (200 mg) 2) Control	sleep (PSQI): reduction on day 45, day 90 compared to baseline and the placebo group ($p < 0.001$); stress (PSS-14): reduction on days 45, 90 compared to baseline and placebo ($p < 0.001$ at day 90); increase in salivary melatonin, decrease in salivary cortisol and plasma orexin A compared to placebo; increase IgG and IgM; CD4+ count, CD4/CD8 ratio increased, CD8+ cells decreased, total leukocytes, lymphocytes, monocytes increased, neutrophils and eosinophils decreased, IL-1β and IL-2 increased, IL-10 decreased
Salem et al. (2023)	capsules	24	1) *N. sativa* (0.5 g) 2) *N. sativa* (1 g) 3) *N. sativa* (2 g) 4) Control: activated charcoal (162 mg)	group 2 (1 g): elevation compared to baseline in absolute lymphocyte count ($p = 0.008$), CD3+ T-lymphocytes ($p = 0.009$), CD4+ T-helper cells ($p = 0.002$), decrease in diastolic blood pressure compared to baselines; group 1 (0.5 g): decrease in heart rate, systolic blood pressure
Sallam (2009)	capsules	24	1) *N. sativa* (500 mg) 2) Contol: corn starch	decrease in Disease Activity Score, Ritchie Articular Index, morning stiffness, WBC count compared to the placebo phase
Tavakoli-Rouzbehani et al. (2022)	soft gels (2 g daily)	3	1) *N. sativa* oil 2) placebo: sunflower oil	serum levels of sICAM-1 (- 132.38 ng/mL, $p = 0.006$) and sVCAM-1 (- 264.44 ng/mL, $p = 0.044$) decreased, MDA levels declined (- 0.21 nmoL/mL, $p = 0.026$), TAC increased (0.03 nmoL/mL, $p = 0.014$)
Ahirwar et al. (2018)	EO; paste	no mention	1) EO (1 drop) 2) Triple antibiotic paste	reduction in aerobic ($p = 9.76 \times 10 - 25$) and anaerobic ($p = 6.33 \times 10^{-10}$) CFUs after EO; paste better antibiotic properties/reduction in CFUs

Table 5 continued

Ghitea et al. (2021)	0.8 mL (2 drops)	no mention	1) Staphylococcal infection group 2) *E. coli* infection group 3) Streptococcal infection group 4) Control: no infection or treatment	increase in the phase angle, antibacterial effect comparable to standard allopathic antibiotics; absence of dysbiosis
Amerikanou et al. (2023)	Capsule	10	1) CMEO (200 mg) 2) Control	body weight ($p = 0.008$), % body fat ($p < 0.001$), VFL ($p < 0.001$), BMI ($p = 0.008$), and systolic blood pressure ($p = 0.005$), TG ($p = 0.011$), LDL ($p = 0.006$) and ALT ($p = 0.022$), oxLDL ($p = 0.026$), adiponectin ($p = 0.002$)
Amanlou et al. (2007)	solution (5 drops to the lesion four times daily)	0	1) *S. khuzistanic*a extract 2) S. khuzistanica EO 3) Control: hydroalcoholic solution	pain elimination mean time: group 1) and 2) ($p = 0.0001$) compared to the placebo; complete healing mean duration: in group 1) and 2) ($p = 0.0001$) compared to the placebo
Panahi et al. (2014)	3 drops (twice a day)	10	1) EO 2) 0.3 % ciprofloxacin	reduction in pain severity ($p < 0.001$), number of positive cultures for all tested microorganisms reduced ($p < 0.001$) in both groups, symptoms improved ($p > 0.05$ for between-group differences)
Nasirzadeh et al. (2023)	gel (twice daily)	0	1) *Z. multiflora*-loaded nanostructure lipid carriers and terbinafine 2) Placebo and terbinafine	inflammation (87.5 % vs 35 %), itching (90 % vs 40 %), scaling (95 % vs 70 %); complete disappearance of the lesions in 65 % of intervention versus 7.5 % in the placebo ($p < 0.005$)
Alavinezhad et al. (2018)	Capsules	5	1) carvacrol (1.2 mg/kg/day) 2) Placebo	pulmonary function, reduction in respiratory symptoms (day wheeze and exercise wheeze) compared to baseline; total WBC, monocytes, eosinophils, CRP reduced ($p < 0.001$), hematocrit (decrease) and MCHC (increase) at month 1

Table 5 continued

Ghorani et al. (2021)	capsules	0	1) carvacrol (1.2 mg/kg/day) 2) Placebo	respiratory symptoms: night wheeze, chest wheeze, night cough decreased ($p < 0.05$ to $p < 0.001$); pulmonary function tests: FVC, PEF, MMEF values increased ($p < 0.05$ to $p < 0.001$); oxidative stress: MDA, nitrite decreased, SOD activity, thiol content increased ($p < 0.05$ to $p < 0.001$); mCytokines: IL-10 and IFN-γ increased, IL-4 levels decreased, PBMC supernatant ($p < 0.05$ to $p < 0.001$); IFN-γ/ IL-4 ratio increased
Seol et al. (2016)	inhalation (one time)	no mention	1) non-CTS control 2) non-CTS with linalool 3) CTS control 4) CTSwith linalool	DPPH inhibition higher in both experimental groups; reduced systolic blood pressure, diastolic blood pressure and pulse rate in the CTS group, pulse rate in the non-CTS group
Newman et al. (2022)	Mouthrinse	38	1) EO, ctylpyridinium chloride, sodium hydroxide, potassium phosphate monobasic, cinnamaldehyde 2) Control: steril water, cinnamaldehyde	lower supragingival PI at 6 and 12 weeks ($p = 0.022$); altered supragingival microbiome community structure at 12 weeks ($p = 0.001$); depleted supragingival plaque microbiome consortium ($p = 0.017$)

Table 6: Jadad Score

Reference	Question 1	Question 2	Question 3	Question 4	Question 5	Jadad score
Eshwar et al. (2016)	1	1	1	1	1	**5**
Saeidi et al. (2024)	1	1	1	0	0	**3**
Casetti et al. (2012)	1	0	1	0	0	**2**
Duijker et al. (2015)	1	1	1	1	1	**5**
Morovati et al. (2019)	1	1	1	1	1	**5**
Zhuang et al. (2009)	1	0	1	1	1	**4**
Asih et al. (2021)	1	1	0	0	1	**3**
Maddocks-Jennings et al. (2009)	1	0	1	0	1	**3**
Botelho et al. (2009)	1	1	1	1	1	**5**
Beheshti Roy et al. (2014)	1	1	1	1	1	**5**
Dryden et al. (2004)	1	1	0	0	1	**3**
Joksimovic et al. (2012)	1	1	1	1	0	**4**
Khalil et al. (2004)	1	0	0	0	0	**1**
Pearce et al. (2005)	0	0	0	0	1	**1**
Taalab et al. (2021)	1	1	0	0	1	**3**
Mazzarello et al. (2020)	1	0	0	0	1	**2**
Hi and En-dang (2020)	1	0	0	0	1	**2**
Majeed et al. (2024)	1	1	1	1	1	**5**
Mohan et al. (2023)	1	1	1	1	1	**5**
Salem et al. (2023)	1	1	1	1	1	**5**
Sallam (2009)	0	0	0	0	1	**1**

Table 6 continued

Tavakoli-Rouzbehani et al. (2022)	1	1	1	1	1	**5**
Ahirwar et al. (2018)	1	0	0	0	0	**1**
Ghitea et al. (2021)	0	0	0	0	1	**1**
Amerikanou et al. (2023)	1	1	0	0	1	**3**
Amanlou et al. (2007)	1	0	1	1	1	**4**
Panahi et al. (2014)	1	1	0	0	1	**3**
Nasirzadeh et al. (2023)	1	0	1	0	1	**3**
Alavinezhad et al. (2018)	1	1	1	0	1	**4**
Ghorani et al. (2021)	1	1	1	0	1	**4**
Seol et al. (2016)	1	0	1	0	0	**2**
Newman et al. (2022)	1	1	1	1	1	**5**

Note: Question 1 = Was the study described as randomized? (Yes: 1; No: 0)
Question 2 = Was the method of randomization appropriate? (Yes: 1; No: 0)
Question 3 = Was the study described as blinded? (Yes: 1; No: 0)
Question 4 = Was the method of blinding appropriate? (Yes: 1; No: 0)
Question 5 = Was there a description of withdrawals and drop-outs? (Yes: 1; No: 0)

3.2 Systemic Immune Modulation and Oxidative Stress

Metabolic syndrome represents a complex pathophysiological constellation of risk factors, comprising visceral obesity, insulin resistance, type 2 diabetes mellitus, arterial hypertension, and dyslipoproteinemia. The greater the number and severity of these risk factors, the higher the patient's overall cardiovascular risk is. A central pathomechanism of the metabolic syndrom is chronic systemic inflammation. This inflammatory state is characterized by an elevation of pro-inflammatory cytokines, like TNF-α and IL-6. These cytokines reduce insulin sensitivity and influence T-cell regulation within the gut-associated lymphoid tissue. Consequently, a multifactorial treatment approach focused on weight normalization and the management of diabetes, hypertension, and dyslipidemia is needed to reduce cardiovascular risk [Pape et al., 2023].

3.2.1 Systemic Immunomodulation and Autoimmunity

To evaluate the therapeutic effects of *N. sativa*, an in-vivo experimental animal model combined with a sequential, placebo-controlled clinical trial was performed. The clinical phase involved female rheumatoid arthritis patients who were already maintained on a standard background therapy of methotrexate, hydroxychloroquine, and folic acid. Out of the 60 initially recruited patients, 24 dropped out. Over a timeframe of four weeks, the patients participated in a single-arm sequential design. They received a corn starch placebo capsule twice daily for the first two weeks, followed by 500 mg *N. sativa*. The results showed that after receiving *N. sativa*, there was a significant decrease in their Disease Activity Score, Ritchie Articular Index, morning stiffness, and white blood cell (WBC) count compared to their baseline measurements during the placebo phase [Sallam, 2009].

In another study, the effects of *N. sativa* were evaluated after four weeks of oral administration on healthy students. They measured the heart rate, systolic and diastolic blood pressure, mean arterial pressure, immune parameters (absolute lymphocyte count, CD3+ T-lymphocytes, CD4+ T-helper cells, CD8+ T-suppressor cells, CD19+ B-lymphocytes, natural killer (NK) cells, and CD4+/CD8+ ratio), immunoglobulins and cytokines (IgG, IgM, IL-1beta, IL-4, IL-6, IL-10, TNF), and gene expression (IFN- γ, NF-B, TNF-, IL-1β, IL-13, IL-8, IL-6). 76 participants were randomly divided into receiving either 0.5 g, 1 g, or 2 g of *N. sativa* capsules, or 162 mg of activated charcoal capsules (placebo). Only the 1 g dose of *N. sativa* produced a significant elevation compared to baseline in absolute lymphocyte count ($p = 0.008$), CD3+ T-lymphocytes ($p = 0.009$) and CD4+ T-helper cells ($p = 0.002$). Interestingly, this elevation in T-cells was lost when the dose was increased to 2 g. Regarding vital signs, the 0.5 g *N. sativa* group showed a decrease in heart rate and systolic blood pressure. The 1 g *N. sativa* group showed a significant decline in diastolic blood pressure compared to their baselines. However, there were no significant changes observed in immunoglobulins, cytokines, or gene expressions across any of the groups [Salem et al., 2023].

In the study by Mohan et al. (2023), authors investigated the effect of a black cumin oil extract on the stress-sleep-immunity axis. Thymoquinone was considered as the most active constituent. The 90-day study included 72 healthy adults aged 25 to 65 years who complained of sleep problems and stress. Participants received either a 200 mg capsule of the extract or a placebo each evening. The results showed that the consumption of black cumin oil extract led to a significant improvement in sleep quality (measured by the Pittsburgh Sleep Quality Index, PSQI) and a reduction in subjective stress levels (measured via the Per-

ceived Stress Scale, PSS-14) after both 45 and 90 days. These positive effects were also reflected in a significant increase in sleep-promoting hormone melatonin, a significant decrease in the stress hormone cortisol and the neuropeptide orexin A in the plasma. Furthermore, the intervention demonstrated immunomodulatory properties. Serum levels of the immunoglobulins IgG and IgM, the total number of leukocytes, lymphocytes, monocytes, and CD4+ cells increased significantly, leading to an improved CD4/CD8 ratio. CD8+ cells, neutrophils, and eosinophils decreased. The levels of the pro-somnogenic cytokines IL-1β and IL-2 increased, whereas the anti-somnogenic cytokine IL-10 decreased [Mohan et al., 2023].

3.2.2 Oxidative Stress and Endothelial Inflammation

To evaluate the effect of *N. sativa* oil on endothelial function in patients with stable coronary artery disease (CAD), 49 patients undergoing angiography who presented with at least 50 % stenosis in one or more main coronary arteries were enrolled. Endothelial function was assessed with the help of adhesion molecules, atherogenic indices, lipid profile ratios, and markers of oxidative stress. Soluble adhesion molecules, such as intercellular adhesion molecule-1 (sICAM-1) and vascular cell adhesion molecule-1 (sVCAM-1), are established predictors of future fatal cardiovascular events. They are also linked to the progression of atherosclerosis in patients with CAD. The results showed a reduction in sICAM-1 (-132.38 ng/mL, $p = 0.006$) and sVCAM-1 (-264.44 ng/mL, $p = 0.044$) compared to the placebo group. Additionally, *N. sativa* oil reduced MDA levels (-0.21 nmoL/mL, $p = 0.026$). The increase in TAC was only significant when compared to the placebo group (0.03 nmoL/mL, $p = 0.014$). The authors attributed these results primarily to the oil's main active constituent, thymoquinone [Tavakoli-Rouzbehani et al., 2022].

The efficacy of Chios Mastiha EO (CMEO) -derived from the resinous exudate of *Pistacia lentiscus*- as an adjunct to conventional medication in patients suffering from abdominal obesity and concurrent metabolic abnormalities, such as dyslipidemia, hypertension, and insulin resistance was analyzed. The hypothesis was that the high bioavailability of CMEO's monoterpenes would have a positive impact on serum oxidative resistance and thereby counteracting the systemic inflammatory processes. Following a three-month intervention, clinical outcomes demonstrated a significant decrease in body weight, BMI, total body fat percentage, and visceral fat levels (VFL). Furthermore, reductions in systolic blood pressure, triglycerides, LDL, and alanine aminotransferase (ALT), indicating improved hepatic health were observed. The treatment declined oxidized LDL (oxLDL) and showed an elevation of adiponectin. There was also a patient's reported enhancement in their overall well-being, measured with the help of physical (PCS-12) and mental (MCS-12) composite scores, which assess their quality of life [Amerikanou et al., 2023].

In another study, the effects of *Cuminum cyminum* EO on patients with increased waist circumference, elevated blood pressure, elevated triglycerides, reduced high-density lipoprotein (HDL), and/or elevated fasting glucose were investigated. Patients in the intervention group consumed 75-mg soft gel of the EO three times daily. Blood levels of malondialdehyde (MDA), superoxide dismutase (SOD), total antioxidant capacity (TAC), catalase (CAT), glutathione peroxidase (GSH-Px), CRP, and TNF-α were measured. The results showed an improvement in SOD ($p = 0.001$), TAC ($p = 0.002$), and MDA ($p = 0.01$) [Morovati et al., 2019].

The effect of black seed oil derived from *N. sativa*, with a standardized thymoquinone content of 2.72 %, was evaluated in patients with metabolic syndrome. 62 eligible patients, who met at least three of the five criteria for metabolic syndrome (such as abdominal obesity, hyperglycemia, hypertension, dyslipidemia, or low HDL) were analyzed. The treatment group received 3 mL/day black seed oil, and the control group received a placebo alongside standard therapy. The primary endpoint evaluated was the level of nuclear factor erythroid 2-related factor 2 (Nrf2). Ultimately, the results demonstrated no significant effects [Hi and Endang, 2020].

Carpal tunnel syndrome (CTS) is a peripheral neuropathy and ischemic-reperfusion injury, with oxidative stress considered to be a major underlying cause. To investigate the potential therapeutic effects of linalool, a clinical study compared subjects with and without CTS who were assigned either to a ten-minute inhalation of linalool or to a respective control group. The mean DPPH (2,2-diphenyl-1-picrylhydrazyl) radical-scavenging activities in plasma samples from the non-CTS control, non-CTS linalool, CTS control, and CTS linalool groups were 10.40 ± 3.08 %, 30.38 ± 1.32 %, 16.32 ± 3.39 %, and 27.36 ± 1.82 %, respectively. This DPPH radical scavenging activity was significantly higher in the CTS linalool group compared to its respective control group ($p = 0.031$) and in the non-CTS linalool group compared to its control group ($p < 0.001$). Following the inhalation of linalool, both systolic ($p = 0.004$) and diastolic ($p = 0.025$) blood pressure decreased significantly from baseline in subjects with CTS, although there were no significant differences observed among the four groups overall. Similarly, the inhalation of linalool significantly reduced heart rate compared to baseline in both the non-CTS linalool ($p = 0.004$) and CTS linalool ($p = 0.017$) groups, though again, there were no significant differences among the four groups after the intervention [Seol et al., 2016).

3.3 Supportive Care in Oncology (Mitigating Therapy-Induced Immunosuppression)

In oncology, chemotherapy refers to the use of cytotoxic substances (cytostatics) for the medical treatment of cancer. The aim of these drugs is to inhibit the growth of cancer cells as specifically as possible to slow down tumor progression or bring it to a complete halt. However, since these cytotoxic substances also attack healthy body cells, this results in the typical side effect profile of the treatment [Fehm et al., 2021; Riemann et al., 2019].

Whether side effects occur and how severe they are varies individually. This depends, among other things, on the type of medication used, the dosage and the duration of treatment. In addition, cancer itself can put a heavy strain on the organism and be accompanied by various symptoms. To prevent or treat these side effects, medical doctors use targeted supportive medications (supportive therapy), which often also include "off-label use" [Leitlinienprogramm Onkologie, 2018].

To investigate the effects of citronellol in combination with a Chinese medical herb complex on the cellular immunity of cancer patients receiving chemotherapy and/or radiotherapy, a six-week randomized, placebo-controlled trial was performed. 105 patients were enrolled and assigned to either an experimental group receiving the herbal intervention or a control group receiving a matching placebo. The results demonstrated that the intervention mitigated the immunosuppressive side effects, which are typical of cancer treatments. Specifically, the intervention group showed a significantly lower depletion of leukocytes (a 14.2 % loss

compared to 28.2% in the placebo group) and neutrophils (an 11.0 % loss compared to 29.1 % in the placebo group). Additionally, the intervention helped preserve hematocrit, platelet concentrations, CD4 lymphocytes and NK cells, which significantly decreased in the placebo group [Zhuang et al., 2009].

Another study investigated the therapeutic effects of a mouthwash containing manuka (Leptospermum scoparium) and kanuka (Kunzea ericoides) EO on radiation-induced mucositis. The trial included 21 adult patients undergoing at least four weeks of non-palliative radiotherapy for head and neck cancers. Participants were assigned to one of three arms: an active group gargling a 1:1 EO-mix diluted in water, a placebo group gargling sterile water or a control group receiving only usual care. The intervention started on or up to two days before the first day of radiotherapy and continued for one week after its completion. The results demonstrated that the EO gargle significantly delayed the onset of mucositis. Patients in the active group developed their first mucositis reaction at a mean radiation dose of 3120 cGy, which was significantly later than the placebo group (1450 cGy) and the control group (2163 cGy) ($p = 0.05$). Furthermore, the active group exhibited less weight loss (only a 1 % decrease compared to 4.5 % for placebo and 2.5 % for control) and reported lower pain levels as well as reduced analgesic medication. However, these secondary findings did not reach statistical significance due to the small sample size. The study also noted that patients with full dentures had significantly lower overall mucositis scores than those who required dental extractions prior to treatment ($p = 0.023$) [Maddocks-Jennings et al., 2009].

3.4 Infection Control and Localized Inflammation

A wound is defined as a disruption of tissue continuity on external or internal body surfaces, occurring with or without associated tissue loss. When a clinically manifest wound infection develops, it typically presents with classical local symptoms: pain, erythema, localized warmth, swelling, pathological exudation, and a foul odor. Furthermore, these local indicators are frequently accompanied by systemic manifestations, such as fever and lymphadenopathy. In modern clinical practice, there is a growing global trend of chronic wounds becoming contaminated with multidrug-resistant pathogens, most notably methicillin-resistant *Staphylococcus aureus* (MRSA). While the exact extent to which mere bacterial contamination delays the wound healing process remains a subject of scientific debate, the logistical and therapeutic consequences of an MRSA diagnosis are profound for both the patient and the healthcare institution. Should a subsequent systemic MRSA infection ensure, it poses a severe clinical challenge due to the current scarcity of effective reserve antibiotics. To preserve these critical systemic therapies, effective localized decolonization strategies are urgently needed. In this context, topical phytotherapy -particularly the application of EO- has gained substantial scientific traction as a promising approach to reduce local microbial bioburden without exerting further selection pressure for antimicrobial resistance [Dissemond et al., 2005; AWMF, 2025]

The immune system protects the organism by eliminating antigens, such as pathogens, foreign substances and tumor cells, while maintaining tolerance toward healthy endogenous structures. It is divided into the innate (non-specific) defense, which acts as the immediate first line of response comprising phagocytes, NK cells, mast cells, the complement system and cytokines. The adaptive (specific) defense develops tailored mechanisms, including B- and T-lymphocytes and antibodies CRP is an acute-phase protein, which is used as a sensitive biomarker for inflammatory processes, because of its rapid increase in plasma during acute reactions (doubling approximately every eight hours) and decrease once the stimulus is re-

moved. This allows a precise monitoring of disease progression and therapeutic response [Wesker and Fisahn, 2023].

3.4.1 Respiratory and Otic Infections

In a double-blind, randomized controlled trial adult patients (≥ 18 years) suffering from upper respiratory tract infections were investigated. The active intervention consisted of EO derived from three traditional Cretan herbs (*Coridothymus capitatus, Salvia fruticosa,* and *Origanum dictamnus*) mixed in extra virgin olive oil. The researchers measured the severity and duration of symptoms using the Wisconsin Upper Respiratory System Survey. The systemic inflammation was measured via CRP status. Ultimately, the intervention did not demonstrate a significant benefit over the placebo. While an exploratory subgroup analysis of virus-positive patients indicated that 90 % of the treated cohort were symptom-free by day seven compared to 70 % in the control group, this secondary finding requires cautious interpretation. However, within the intervention group, the normalization of CRP levels by the end of the follow-up period was found to be significant [Duijker et al., 2015].

In another study, the efficacy of an EO combination was compared to standard ciprofloxacin 0.3 % ear drops for the treatment of acute external otitis (AEO). The EO was gathered from *Syzygium aromaticum*, *Lavandula angustifolia*, and *Geranium robertianum*, with the primary active components eugenol, linalool, geraniol, and citronellol. Following the intervention in patients who showed initial symptoms of AEO, the results demonstrated that both groups experienced a significant reduction in pain severity ($p < 0.001$) and decrease in the number of positive microbial cultures ($p < 0.001$). The statistical analysis revealed no significant differences in symptom improvement between the two treatment groups ($p > 0.05$) [Panahi et al., 2014].

3.4.2 Skin and Wound Infections

To evaluate the efficacy of topical tea tree oil preparations compared with a standard topical regimen, 224 hospitalized patients with confirmed MRSA colonization were enrolled in a study. The intervention group received a treatment consisting of 10 % tea tree nasal cream, 5 % tea tree body wash, and 10 % tea tree cream for skin lesions. The control group was treated with a standard regimen of 2 % mupirocin nasal ointment, 4 % chlorhexidine gluconate soap, and 1 % silver sulfadiazine cream. Both treatments were administered for five days. The results showed no significant difference between the two groups regarding total MRSA eradication. The clearance rate for the standard treatment was 49 %, whereas the tea tree group achieved 41 %. However, the clearance of nasal carriage showed a significant difference. Mupirocin was more effective with a clearance rate of 78 % compared with 47 % for the tea tree nasal cream. The clearance of MRSA from skin sites and wounds showed no significant difference between the groups. This indicates comparable, albeit non-superior, outcomes in these specific areas [Dryden et al., 2004].

Ghitea et al. (2021) used *Origanum vulgare* EO in patients with metabolic syndrome suffering from minor, uncomplicated *S. aureus*, *Escherichia coli*, or *Streptococcus pyogenes* infections. Patients consumed 0.8 mL (two drops) of EO twice daily for 10 days. The number of infections across all three patient groups decreased when compared with their baseline evaluations. Furthermore, the phase angle, which is an indicator of cellular function and health, improved in the intervention groups. The treatment did not trigger intestinal dysbio-

sis (measured by symptoms like diarrhea, flatulence, and gastrointestinal pain), which is often associated with standard broad-spectrum antibiotics [Ghitea et al., 2021].

In another study, the antibacterial activity and skin tolerance of coriander EO were investigated. An in-vitro macrodilution assay was performed to evaluate the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of the EO against clinically relevant dermatological bacteria. Its efficacy was compared with standard reference antibiotics. The results showed growth inhibition across most tested strains, particularly against *S. pyogenes* (MIC 0.04% v/v), *S. viridans* (MIC 0.08% v/v), and MRSA (MIC 0.25% v/v). Skin tolerance and irritation potential were assessed in 40 healthy volunteers using a 48-hour occlusive patch test. All 40 participants were tested with six different preparations on their backs: 0.5 % EO lotion, 1.0 % EO lotion, 0.5 % EO cream, 1.0 % EO cream, placebo lotion and placebo cream. The application followed an alternating sequence. Photometric evaluations revealed no significant changes in erythema, indicating that the EO possessed no irritant effects [Casetti et al., 2012].

In a clinical trial, the efficacy of a topical gel for treating mild to moderate cutaneous dermatophytosis was investigated. The study used nanostructured lipid carriers (NLCs) loaded with the EO of *Zataria multiflora*. 80 participants who had both clinical and mycological diagnoses of dermatophytosis were enrolled in this study. Participants were equally divided into two groups, receiving either a 1 % *Z. multiflora* NLC gel or a placebo gel. Both groups applied their gel twice daily while also receiving standard topical terbinafine treatment. After four weeks of treatment, the *Z. multiflora* NLC group showed a greater reduction in inflammation (87.5 %), itching (90 %), and scaling (95 %) compared with the control group. Complete resolution of the skin lesions was observed in 65 % of the experimental group versus 7.5 % of the control group ($p < 0.005$) [Nasirzadeh et al., 2023].

3.4.3 Inflammatory Skin and Tissue Conditions

The effectiveness of an herbal gel containing *Berberis integerrima* root extract and spearmint (*Mentha spicata*) EO was evaluated in the treatment of acne vulgaris. The study included 75 patients with mild to moderate facial acne who were divided into two groups. The intervention group received a gel with 5 % *B. integerrima* root extract and 1 % spearmint EO, whereas the control group received 1 % clindamycin gel. After using the gels twice daily for eight weeks, there was a significant reduction in the number of acne lesions ($p < 0.001$) and Modified Global Acne Grading System (mGAGS) scores ($p < 0.001$) in both groups. There was no significant difference in efficacy between the intervention and the clindamycin control, suggesting that the gel is a viable natural alternative for acne management [Saeidi et al., 2024].

Another study investigated the anti-acne efficacy and anti-inflammatory properties of a topical cream containing EO combined with tretinoin. The EO was gathered from *Myrtus communis* and *O. vulgare*. The trial enrolled 60 participants who suffered from mild-to-moderate facial acne and had not used topical or systemic therapies for at least three months. The intervention group received the experimental formulation comprising 3.74 % *M. communis* EO, 0.1 % *O. vulgare* EO, and 0.025 % tretinoin. The control applied a commercial clindamycin and tretinoin gel. Efficacy was evaluated over a 30-day time frame, with assessments at baseline, day 15, and day 30. The results showed that both treatments reduced the number

of acne lesions. Transepidermal water loss also increased in both groups. Starting from day 15, the EO cream improved papular erythema compared with the control gel ($p = 0.0329$) and reduced retinoid-induced rashes on healthy perilesional skin. Erythema on healthy skin increased in the control group at day 30 ($p = 0.0017$). However, there was no significant difference between the two groups regarding overall clinical improvement [Mazzarello et al., 2020].

To evaluate the therapeutic efficacy and tolerability of a 5 % *Melaleuca alternifolia* (tea tree) EO gel for the treatment of mild to moderate facial seborrheic dermatitis, 54 patients were enrolled in a four-week study. The intervention group was treated with a 5 % tea tree oil gel, whereas the control group received a placebo gel. Participants were instructed to apply their gel to the affected facial areas three times daily. Clinical assessments of itching, erythema, scaling, greasy crusts, patient satisfaction, and side effects were performed after the second and fourth weeks. The results showed that at both time points, the intervention group exhibited significant improvements compared with the placebo group. These results were reflected in patient satisfaction scores, which indicated a "total cure" in 91 % of patients by the fourth week. The placebo group reported no such improvements. Additionally, no allergic irritation or inflammation was observed in either group throughout the study [Beheshti Roy et al., 2014].

Furthermore, the efficacy of a topical EO blend as an antipruritic agent for pregnant women experiencing moderate to severe itching was investigated. The 14-day study included 57 pregnant women (at 25 to 38 weeks of gestation). The intervention group applied a blended oil, consisting of 1 % peppermint oil, 1 % lavender EO, and 1 % essential turmeric oil mixed in virgin coconut oil, twice daily after bathing. The control group applied pure virgin coconut oil. The results demonstrated that the intervention led to a significant reduction in pruritus and pruritus severity, with Visual Analog Scale scores dropping from a baseline average of 62.7 mm to 22.4 mm ($p < 0.001$) [Asih et al., 2021].

Haemorrhoids are linked to a disruption in collagen metabolism, which is evidenced by lower collagen levels in affected patients. The condition is characterized by mucosal inflammation, which typically presents as bleeding, tissue prolapse, and anal pain that notably intensifies during bowel movements. To investigate potential treatments, a two-week trial involving 36 patients with grade I–III hemorrhoids was conducted. The participants were divided into two equal groups, receiving an active treatment gel (containing hyaluronic acid, tea tree oil, and methylsulfonylmethane) or a placebo gel. The results from the intervention group showed a decrease ($p < 0.001$) from baseline in patient-reported pain during evacuation, pruritus, irritation, and visible bleeding. General pain, inflammation, and visible bleeding, which were based on investigator evaluation, were also reduced. Interestingly, the placebo treatment also demonstrated some symptom relief, indicating that the application of a gel may partially alleviate haemorrhoid symptoms [Joksimovic et al., 2012].

3.5 Dental and Oral Mucosal Immunity

Oral pathogenic bacteria can disseminate into the organism both hematogenously via the bloodstream and pulmonarily via the respiratory tract, triggering systemic inflammatory responses. This process significantly increases the risk of serious secondary diseases. Additionally, the oral cavity undergoes a physiological aging process. The oral mucosa loses elasticity and thickness, rendering it clinically more vulnerable to mechanical insults and infections.

The central clinical condition in this context is periodontitis, a bacterially induced, chronic inflammatory disease of the periodontium. Given the systemic impact of periodontitis, the therapy has a crucial role in general health. It not only resolves local inflammation but also demonstrably reduces the levels of systemic inflammatory markers [Borgart, 2023; Petring, 2025].

3.5.1 Periodontal Disease and Gingival Inflammation

In a clinical trial, the antimicrobial and clinical efficacy of a 1% *Lippia sidoides* EO mouthrinse compared to a standard 0.12 % chlorhexidine mouthrinse was analyzed. 55 eligible participants with a minimum baseline plaque index (PI) and gingival index (GI) were enrolled and randomly assigned to rinse twice daily with their respective solutions for seven days. The primary endpoints, evaluated at baseline, seven days, and 30 days, included salivary *Streptococcus mutans* colony counts, PI, GI, and gingival bleeding indices. The results indicated that both mouthrinses significantly reduced *S. mutans* salivary counts and all evaluated periodontal indices after both seven and 30 days compared to baseline. Importantly, there were no significant differences between the EO group and the chlorhexidine group [Botelho et al., 2009].

To investigate and compare the efficacy of a 0.5 % dill seed oil (*Anethum graveolens*) mouthrinse with that of a standard 0.12 % chlorhexidine mouthrinse in reducing plaque and gingivitis, a clinical trial was performed. The 15-day study involved 60 healthy dental students exhibiting baseline plaque and gingivitis. Clinical assessments of PI and modified GI were performed at baseline, after 5, 10, and 15 days. The results showed that both mouthrinses led to a reduction in plaque and gingivitis scores over the 15-day period ($p < 0.05$). Furthermore, the between-group analysis revealed no significant differences between the two mouthrinses [Eshwar et al., 2016].

Another study analyzed a mouthrinse with cetylpyridinium chloride (CPC) and EOs (menthol, eucalyptol, methyl salicylate, and thymol). Healthy participants with at least 20 gradable teeth and ten or more bleeding sites were randomized. They were assessed at baseline, six weeks, and 12 weeks. Despite a 29 % dropout rate, the study met its endpoint, demonstrating that the intervention significantly reduced supragingival plaque scores in 6 and 12 weeks compared to the control. The secondary microbiome assessments revealed that the treatment altered and depleted the supragingival microbiome community structure. However, while both study arms showed significant improvements in GI, there was no significant difference between the two groups. There was also no significant improvement in bleeding on probing (BOP) or pocket probing depth (PPD) [Newman et al., 2022].

Taalab et al. (2021) included 30 patients who were diagnosed with Stage II periodontitis. The participants were divided into two groups: a control group that received scaling and root planing (SRP) alone, and an intervention group that received SRP combined with the local application of a 5 % tea tree oil gel. SRP involves smoothing the root surfaces to minimize bacterial adherence, and to facilitate the reattachment of healthy gingival tissue. PPD, clinical attachment level (CAL), GI, and BOP showed significant improvements from baseline through all follow-up periods in both groups. However, the intervention group showed superior clinical outcomes. Specifically, at six months, a difference in mean CAL ($p = 0.004$) and mean percentage reduction in CAL ($p = 0.003$) were found between the two groups. At both three and six months, there was a difference in the mean GI ($p = 0.005$) and mean percent-

age reduction in GI ($p = 0.029$ and $p = 0.001$, respectively). Furthermore, a difference was observed in the mean BOP between the groups ($p = 0.002$) and mean percentage reduction in BOP ($p = 0.001$). Gingival crevicular fluid matrix metalloproteinase-8 (MMP-8) levels showed a significant reduction from baseline through all follow-up periods in both groups. At six months, a decrease in MMP-8 levels was found in the tea tree oil group compared with the control group ($p = 0.005$) and the mean percentage reduction in MMP-8 levels was greater in the tea tree oil group at three and six months ($p = 0.003$ and $p < 0.001$, respectively) [Taalab et al., 2021].

3.5.2 Oral Ulcers and Endodontic Infections

To analyze and compare the efficacy of Satureja khuzistanica extract, its EO, and a water-alcohol control solution, a trial which included 60 patients with recurrent aphthous stomatitis who presented with active ulcerations (minor aphthae) on the oral mucosa was performed. The results showed that both the extract and EO treatments differed significantly from the control group ($p = 0.0001$) regarding the average time required for complete healing of the lesions and the elimination of pain. However, there was no significant difference in efficacy between the extract and the EO groups [Amanlou et al., 2007].

In a clinical study, the aerobic and anaerobic antimicrobial efficacy of EO from *Ocimum sanctum* was investigated in comparison to a triple antibiotic paste as an intracanal medicament in the root canals of primary molars. The study involved 40 children aged four to nine years, whose primary molars exhibited clinical and radiographic signs of periapical abscesses or fistulas, and whose roots were at least two-thirds intact. The patients were randomly divided into two equal groups ($n = 20$ each): the first group received a drop of the EO directly into the root canal, while in the second group, the canal walls were coated with the paste (consisting of metronidazole, ciprofloxacin, and minocycline in propylene glycol). Microbiological samples were taken from the apical third of the root at three time points: after the initial access cavity preparation, after irrigation with saline solution and three days after the placement of the respective medicament. The results showed that the application of the EO led to a significant reduction in both aerobic ($p = 9.76 \times 10^{-25}$) and anaerobic ($p = 6.33 \times 10^{-10}$) colony-forming units (CFUs) after three days. Furthermore, it was found that irrigation with saline solution alone, prior to the administration of the medicament, significantly reduced the bacterial load in both groups. In a direct comparison of the two preparations, however the triple antibiotic paste proved to be even more effective and resulted in a significantly greater microbial reduction than the EO. The authors concluded that while the antibiotic paste possesses superior antimicrobial properties, the EO of *O. sanctum* represented a potent and effective alternative. Due to its strong antibacterial and anti-inflammatory effects, as well as the absence of the risk of developing antibiotic resistance, it seems to be a promising herbal medicament, especially for long-standing infections of primary teeth [Ahirwar et al., 2018].

3.6 Immune-Related Hypersensitivities and Allergies

The prevalence of immediate-type allergic diseases (Type I allergies), including allergic asthma, allergic rhinitis, food allergies, and anaphylaxis, is increasing worldwide. After contact with an allergen, B cells are stimulated by CD4+ Th2 cells to produce antigen-specific immunoglobulin E (IgE) antibodies. This initiates an immediate allergic reaction and subsequently leads to the activation of mast cells and basophils. Their ensuing degranulation causes the release of various inflammatory mediators as well as the production of the Th2 cytokines IL-

4 and IL-13. Current standard therapies for Type I allergies are based on corticosteroids and antihistamines. However, these are not effective in all cases and are often accompanied by various side effects [Anastasiou and Buchbauer, 2017]. Therefore, there is a need for immunomodulators to effectively manage Type I allergies with minimal adverse effects. In this context, EOs are increasingly being investigated for their therapeutic potential.

3.6.1 Allergic Airway Diseases (Asthma and Rhinitis)

Allergic rhinitis is an IgE-mediated inflammatory disease of the nasal mucosa triggered by inhaled allergens. It often manifests during childhood and adolescence, although the symptoms can also naturally regress after adolescence. A clinical diagnosis requires the presence of at least two characteristic symptoms, such as watery rhinorrhea, nasal obstruction, sneezing, or itching, occurring for at least one hour on most days over two consecutive days. Allergic rhinitis is also associated with allergic conjunctivitis and atopic eczema. It is standard to use skin prick tests, nasal provocation tests, and the serological detection of specific IgE antibodies for diagnostic confirmation. The therapeutic focus involves strict allergen avoidance, often in combination with symptomatic management using oral or intranasal antihistamines and intranasal corticosteroids. Furthermore, allergen-specific immunotherapy can modify the underlying immunological response [Guntinas-Lichius et al., 2021; Kerbl et al., 2026].

In a study, the efficacy of *N. sativa* oil (standardized to 5 % thymoquinone) on seasonal allergic rhinitis was investigated. The clinical trial included 65 participants who were diagnosed with seasonal allergic rhinitis and experienced at least two symptoms (such as sneezing, rhinorrhoea, nasal obstruction, and nasal itching) for more than one hour per day. The intervention contained 250 mg capsules of *N. sativa* oil combined with 2.5 mg of piperine. Both groups were instructed to take a capsule twice daily for 15 days. Changes in the Total Nasal Symptom Score (TNSS), Total Ocular Symptom Score (TOSS), serum IgE levels, and the Patient Global Impression of Improvement (PGI-I) were measured. The results showed improvements in the TNSS, TOSS, and PGI-I scales. However, the treatment did not lead to a significant change in serum IgE levels [Majeed et al., 2024].

Asthma is a chronic inflammatory airway disease characterized by bronchial hyperreactivity. The underlying inflammation of the bronchial mucosa is considered to be the actual cause of the condition. In most cases, asthma is triggered by an IgE-mediated, T2-type allergic immune response. The sensitized immune system reacts to external proteins (allergens). This sensitization causes the airways to become hyperresponsive, reacting severely to various environmental stimuli. There is also a less common, non-allergic form. The condition typically follows a variable clinical course, characterized by significant fluctuations in symptom severity over time. A strong indicator of asthma is the sudden onset of shortness of breath (dyspnea) and/or coughing [Kroegel et al., 2024; Petermann, 2004].

Another clinical study investigated the effects of carvacrol in 23 patients with moderate to severe asthma. Over a two-month period, the participants received daily carvacrol capsules (1.2 mg/kg/day) or a matching placebo. The carvacrol group showed significant improvements in the pulmonary function tests, specifically the Forced Vital Capacity (FVC), Peak Expiratory Flow (PEF) and Maximal Mid-Expiratory Flow (MMEF) parameters. Furthermore, there was a reduction in clinical respiratory symptoms, such as daytime and exercise-induced wheezing, compared to the baseline. Blood analysis revealed a significant decrease

in inflammatory markers (CRP), total WBC, monocytes, and eosinophils in the carvacrol group [Alavinezhad et al., 2018].

Ghorani et al. (2021) investigated also the therapeutic effect of carvacrol in patients with asthma. A total of 33 adult patients with mild-to-severe asthma participated in the two-month study. Participants were divided into two groups, receiving carvacrol capsules at a dosage of 1.2 mg/kg/day three times daily or a placebo, both in addition to their regular asthma medication. The Measurements of the study endpoints were conducted at baseline (Day 0) as well as after one and two months. As a result, respiratory symptoms, such as night wheeze (NW), chest wheeze (CW) and night cough (NC) ($p < 0.05$), were reduced by carvacrol. The relief of chest wheeze improved even further over time. Values for pulmonary function tests (FVC, PEF, and MMEF) improved significantly under carvacrol. The percentage increase in these values was also significantly higher than in the placebo group. Further, the concentration of harmful oxidative markers (MDA and nitrite) in serum decreased significantly within the carvacrol group compared to baseline values. After two months, the percentage changes in nitrite were higher in the carvacrol-treated group than in the placebo group ($p < 0.05$). Similarly, protective antioxidant markers (SOD activity and thiol content) increased in the intervention group compared to baseline. The percentage changes in thiol after one and two months were higher than in the placebo group ($p < 0.05$ for both cases). The percentage change in SOD was higher than in the placebo group after two months ($p < 0.01$). No significant changes were observed in CAT activity. Additionally, carvacrol treatment positively modulated the immune system. In serum and PBMC supernatants, levels of the cytokines IL-10 and IFN- γ increased significantly ($p < 0.05$ to $p < 0.001$), while IL-4 levels decreased significantly ($p < 0.05$). The IFN- γ /IL-4 ratio in serum ($p < 0.01$) and in PBMC supernatant ($p < 0.05$) increased in the intervention group after two months. Percentage changes were only significant for IFN- γ in PBMC supernatant after two months compared to the placebo group ($p < 0.01$). Despite the altered cytokine levels in the blood, no significant differences were observed at the genetic level [Ghorani et al., 2021].

3.6.2 Allergic Contact Dermatitis and Histamine Reactions

Another study analyzed the anti-inflammatory properties of tea tree oil and its isolated components in combined human and rodent studies. The human study focused on the regulation of the histamine-induced wheal and flare response, while the rodent study investigated changes in microvascular blood flow (vasodilation) and protein extravasation (edema) in experimentally induced skin blisters in rats. The human study included 40 healthy volunteers who were injected intradermally with histamine (50 µL of a 100 µg/mL solution) on both forearms. The resulting wheal and flare responses were measured at 10-minute intervals for 60 minutes. At 10 and 20 minutes after the injection, 25 µL of one of four undiluted preparations (tea tree oil, terpinen-4-ol, 1,8-cineole, or α-terpineol) was applied to completely cover the flare and wheal on the test arm. The assignment of test and control arms alternated from subject to subject. Therefore, each participant acted as their own control. The arm receiving the histamine injection without any topical treatment served as the control. The results of the human study showed that both tea tree oil and terpinen-4-ol significantly reduced the histamine-induced wheal and flare response. The rodent study showed that 1,8-cineole reduced microvascular blood flow following sensory nerve stimulation. Terpinen-4-ol, on the other hand, reduced substance P-induced protein extravasation [Khalil et al., 2004].

The effectiveness of topically applied tea tree oil on nickel-induced contact hypersensitivity was evaluated using a trial with 18 subjects with confirmed nickel hypersensitivity. Following exposure to nickel, the participants were treated once on day 3 and a second time on day 5 with either 100 % tea tree oil, a 5 % tea tree oil lotion, a placebo lotion, or 100 % macadamia oil. The study measured the mean erythema index and flare area of skin reactions. The regulatory effects of tea tree oil on the proliferative response of peripheral blood mononuclear cells (PBMCs) to nickel were also analyzed in-vitro. Only the 100 % tea tree oil treatment resulted in significant anti-inflammatory effects. It reduced the mean flare area and the erythematous response compared with nickel-only sites, and it also significantly inhibited the nickel-induced proliferation of PBMCs. The 5 % tea tree oil lotion, placebo lotion, and 100 % macadamia oil had no significant effect [Pearce et al., 2005].

4 Discussion

4.1 Systemic Inflammation, Endothelial Function, and Oxidative Stress

In cohorts with metabolic abnormalities, the chronic low-grade inflammation propagated by visceral adipose tissue significantly impairs endothelial function and immune homeostasis [Pape et al., 2023].

Amerikanou et al. (2023) reported that daily supplementation with CMEO capsules in combination with a standard pharmacological therapy resulted in improved inflammation and oxidative stress markers. The reduction of oxLDL combined with the upregulation of adiponectin, a hormone crucial for mitigating inflammation and enhancing insulin sensitivity, indicates a modulation in oxidative stress and inflammatory pathways [Rydén et al., 2013]. It is possible that CMEO counteracts atherogenic dyslipidemia and diminishes the vascular damage associated with chronic inflammation. This endothelium-protective effect is also shown by Tavakoli-Rouzbehani et al. (2022). They demonstrated that *N. sativa* oil not only significantly reduced serum levels of soluble adhesion molecules (sICAM-1 and sVCAM-1), but also oxidative stress markers (MDA). This downregulation suggests that specific EOs can actively suppress monocyte adhesion to the vascular endothelium and thereby interrupt a critical early step in atherosclerosis progression [Soro-Paavonen et al., 2006; Tavakoli-Rouzbehani et al., 2022]. It is worth noting that Hi and Endang (2020) reported no significant alterations in oxidative stress markers following a short-term administration of black seed oil. However, this finding must be interpreted in light of the trial's low methodological Jadad score.

Morovati et al. (2019) observed an improvement in the antioxidant defense system after *C. cyminum* EO supplementation. Systemic markers, such as SOD and TAC, increased significantly, while MDA concentrations declined. The upregulation of TAC and SOD may help reduce the production of harmful ROS in mitochondria, which is known to cause cell damage [Rydén et al., 2013]. However, the intervention reported no significant impact on the inflammatory markers CRP and TNF-α. This indicates that the systemic inflammation associated with metabolic syndrome remains largely unchanged.

Similarly, Seol et al. (2016) -in a trial yielding a Jadad score of 2- reported that linalool improved the antioxidant activity (indicated by elevated DPPH inhibition) in patients with CTS, a neuropathy frequently complicated by ischemia-reperfusion injury and oxidative stress. Furthermore, linalool achieved a reduction in cardiovascular parameters (systolic blood pressure, diastolic blood pressure and pulse rate), which suggests that the increased antioxi-

dant properties may be associated with dampening the sympathetic tone [Rydén et al., 2013]

4.2 Respiratory Tract Inflammation and Allergic Responses

Majeed et al. (2024) analyzed the efficacy of *N. sativa* oil in patients with allergic rhinitis. The intervention resulted in significant improvements in TNSS and TOSS. Since serum IgE levels remained unchanged, the observed symptom alleviation cannot be attributed to an interruption of primary sensitization or antibody synthesis. The clinical benefits could be explained by modulation of vascular responses or the stabilization of mucosal tight junctions [Nur Husna et al., 2022]. However, further mechanistic studies are required to confirm this hypothesis for *N. sativa* oil.

The results by Ghorani et al. (2021) and Alavinezhad et al. (2018) suggest that carvacrol exerts a dual mechanism in asthmatic patients. On the one hand, it provides symptomatic relief (such as improved pulmonary function and reduced wheezing), and on the other hand, carvacrol seems to act on a systemic level by suppressing leukocyte recruitment and downregulating both inflammatory and oxidative stress pathways. This systemic modulation is relevant for clinical practice, as it indicates that carvacrol might actively mitigate airway narrowing through mucosal decongestion and smooth muscle relaxation [Ghorani et al., 2021; Mims, 2015]. Consequently, it could serve as a valuable, steroid-sparing adjunct in managing chronic airway inflammation.

4.3 Infection Control, Tissue Integrity, and Immune Modulation

In localized infections, tissue granulation usually stalls once the microbial load becomes too high [Bowler, 2002]. When evaluating the trials on localized infections, a critical finding is the non-inferiority of specific EO formulations compared with standard topical antibiotics. Trials evaluating AEO [Panahi et al., 2014] and an EO formulation for acne vulgaris [Saeidi et al., 2024] both demonstrated that EO treatments achieved clinical clearance rates comparable with conventional therapies like 0.3 % ciprofloxacin or 1 % clindamycin. In addition to their broad-spectrum inhibition of common pathogens like *S. aureus* and *S. pyogenes* [Ghitea et al., 2021], these results demonstrate the clinical potential of EOs. In the context of escalating antimicrobial resistance, EOs may provide an effective, non-resistance-inducing strategy to significantly reduce the overprescription of conventional antibiotics in topical and otic care.

Targeting fungal skin infections, Nasirzadeh et al. (2023) reported that a 1 % *Z. multiflora* EO nanogel in combination with terbinafine reduced localized inflammation, itching, and scaling. Khalil et al. (2004) and Pearce et al. (2005) both observed that topical tea tree oil attenuated experimental histamine-induced wheal and flare response. Pearce et al. (2005) also reported a reduction in PBMC hyperproliferation in the nickel contact dermatitis. Sallam (2009) demonstrated that *N. sativa* as an adjunctive administration in rheumatoid arthritis correlated with reduced disease activity scores and leukocyte counts, though this trial scored only 1 on the Jadad scale.

4.4 The Stress-Sleep-Immunity Axis

Mohan et al. (2023) showed that oral supplementation with a black cumin oil extract significantly improved PSQI and PSS in an adult cohort. This intervention correlated with a neuroendocrine shift. The plasma melatonin increased and the stress hormone cortisol declined. Furthermore, the intervention resulted in a pronounced immunological upregulation. Serum levels of IgG and IgM, as well as the absolute counts of CD4+ T-cells were increased, leading

to an improved CD4/CD8 ratio. This suggests that the black cumin oil extract can modulate the neuroendocrine stress response, which has a positive impact on the immune system.

4.5 Oral Mucosal Lesions and Periodontal Disease

Oral conditions are sustained by an imbalance of bacteria and an impaired immune response [Neurath and Kesting, 2024; Radhi et al., 2025]. Clinical trials indicate that EOs may disrupt this axis primarily by lowering the initial bacterial bioburden. For instance, Botelho et al. (2009) showed that a 1 % *L. sidoides* EO-rinse was as effective as 0.12 % chlorhexidine in reducing salivary *S. mutans* and periodontal inflammation over 30 days. Eshwar et al. (2016) showed similar results using a dill seed mouthwash. Furthermore, Newman et al. (2022) demonstrated that treatment with an EO mouthrinse led to a significant reduction in both supragingival dysbiosis and plaque accumulation. Through reduction of the bioburden, EO may limit the cytokine-driven secretion of tissue-degrading MMPs [Neurath and Kesting, 2024]. This mechanism would be in agreement with the study by Taalab et al. (2021), who reported that an adjunctive tea tree oil gel significantly reduced local concentrations of MMP-8.

4.6 Supportive Care in Oncological Interventions

Radiation therapy severely disrupts tissue homeostasis via direct DNA cleavage and organelle dysfunction [King et al., 2016]. In a trial by Maddocks-Jennings et al. (2009), an EO-based gargle solution (*L. scoparium* and *K. ericoides*) delayed the clinical onset of radiation-induced mucositis. The observed delay suggests that the EO solution may help buffer acute free-radical accumulation at the mucosal interface [King et al., 2016].
Zhuang et al. (2009) demonstrated that an oral herbal formulation containing citronellol significantly alleviated the therapy-induced depletion of leukocytes and neutrophils. Critical immune and hematological parameters (CD4+ lymphocyte counts, NK cells, and hematocrit) declined only in the control group. This suggest that the intervention exerts a cytoprotective or hematopoiesis-supporting effect.

4.7 Methodological Limitations and Generalizability

Despite the many documented therapeutic benefits, the reviewed studies showed several limitations that require caution in interpreting these findings.
To begin with, one of the major limitations across the trials was the small sample size. For instance, Pearce et al. (2005) included only 18 participants, which leads to a higher risk of Type II errors. Another limitation is the lack of documented justification for participant withdrawals, as seen in the study by Sallam (2009), where 24 of 60 enrolled subjects dropped out without justification. Furthermore, many trials had short intervention periods (e.g., 10 to 14 days), making it difficult to draw conclusions about long-term use or possible side effects.
Complete blinding was also difficult to achieve in some reviewed studies, particularly in studies investigating topical products. For instance, Asih et al. (2021) compared an EO blend with pure coconut oil without using a method to mask the scent. Another methodological weakness occurs when significant results rely on exploratory *post hoc* analyses rather than primary outcomes, as seen in Duijker et al. (2015). While these observations are helpful in generating hypotheses, they cannot serve as confirmatory clinical evidence. The reliability of the results is also compromised by subjective, self-reported outcome measures (e.g., PSQI and PSS scores).
Also, external validity is limited. Several cohorts consisted of highly specific demographics (e.g., young dental students) that do not reflect the general patient population. Finally, be-

cause EOs are often administered alongside standard pharmacological treatments or in combination with a plant extract, isolating their true therapeutic contribution in everyday clinical practice remains difficult.

5 Conclusion

Aggregated clinical evidence demonstrates the potential of EOs as complementary therapeutics across various subdisciplines. They show efficacy in reducing systemic inflammation and oxidative stress, alleviating respiratory hypersensitivity, and providing localized antimicrobial clearance.

However, these promising findings must be interpreted with caution. For one it is not yet precisely known which specific constituents are responsible for these therapeutic effects. While current scientific consensus assumes that an oil's primary compounds drive its main clinical activity, it is also well documented that a whole EO can exert different pharmacological effects than its isolated individual compounds. Due to the phytochemical complexity, it remains difficult to distinguish the effects of single active agents from broader pharmacological synergies.

Furthermore, recurrent methodological constraints across the reviewed trials, such as small sample sizes, insufficient blinding, and brief intervention periods, currently limit their generalizability. Consequently, robust, large-scale studies remain necessary to establish standardized clinical guidelines.

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8 List of Abbreviation

ACPA Anti-Citrullinated Protein Antibody
ACT Asthma Control Test
AEO Acute External Otitis
ALT Alanine Aminotransferase
AST Aspartate Aminotransferase
BANA Benzoyl-DL-Arginine-Naphthylamide
BMI Body Mass Index
BOP Bleeding on Probing
CAD Coronary Artery Disease
CAL Clinical Attachment Level
CAT Catalase
CD Cluster of Differentiation
CDAI Clinical Disease Activity Index

CFUs Colony-Forming Units
CMEO Chios Mastiha Essential Oil
COX Cyclooxygenase
CPC Cetylpyridinium Chloride
CTS Carpal Tunnel Syndrome
CW Chest Wheeze
DAS Disease Activity Score
DMARDs Disease-Modifying Antirheumatic Drugs
DPPH 2,2-Diphenyl-1-picrylhydrazyl
EO Essential Oil
ESR Erythrocyte Sedimentation Rate
FOXP3 Forkhead-Box-Protein P3
FVC Forced Vital Capacity
GI Gingival Index
GSH-Px Glutathione Peroxidase
HAMD Hamilton Rating Scale for Depression
HDL High-Density Lipoprotein
HMGB-1 High-Mobility-Group-Protein B1
IBDQ Inflammatory Bowel Disease Questionnaire
ICAM-1 Intercellular Adhesion Molecule 1
ICU Intensive Care Unit
IFN- γ Interferon-γ
IgE Immunoglobulin E
IgG Immunoglobulin G
IgM Immunoglobulin M
IL Interleucin
iNOS Inducible Nitric Oxide Synthase
IκBα Inhibitor of Nuclear Factor kappa B alpha
LDL Low-Density Lipoprotein
LOX Lipoxygenase
MBC Minimum Bactericidal Concentration
MCS-12 Mental Component Summary
MDA Malondialdehyde
mGAGS Modified Global Acne Grading System
MIC Minimum Inhibitory Concentration
MMEF Maximal Mid-Expiratory Flow
MMP Matrix Metalloproteinases
MODS Multiple Organ Dysfunction Score
MRSA Methicillin-Resistant *Staphylococcus aureus*
MS Mass Spectrometry *or* Metabolic Syndrome

NC	Night Cough
NF-κB	Nuclear Factor kappa-light-chain-enhancer of activated B cells
NK	Natural Killer (cells)
NLCs	Nanostructured Lipid Carriers
NLRP	Nucleotide-binding oligomerization domain, Leucine-rich repeat, and Pyrin domain containing
Nrf2	Nuclear factor erythroid 2-related factor 2
NW	Night Wheeze
OHI-S	Simplified Oral Hygiene Index
oxLDL	Oxidized Low-Density Lipoprotein
PBMC	Peripheral Blood Mononuclear Cell
PCS-12	Physical Component Summary
PDD	Probing Pocket Depth
PEF	Peak Expiratory Flow
PGI-I	Patient Global Impression of Improvement
PLI	Plaque Index
PSQI	Pittsburgh Sleep Quality
PSS	Perceived Stress
QoL	Quality of Life
RBC	Red Blood Cell
RF	Rheumatoid Factor
ROS	Reactive Oxygen Species
SBI	Sulcus Bleeding Index
Sirt1	Sirtuin 1
SOD	Superoxide Dismutase
SRP	Scaling and Root Planing
TAC	Total Antioxidant Capacity
TC	Total Cholesterol
Th	T helper cells
TNF-α	Tumor Necrosis Factor-alpha
TNSS	Total Nasal Symptom Score
TOSS	Total Ocular Symptom Score
VCAM-1	Vascular Cell Adhesion Molecule 1
VFL	Visceral Fat Level
WBC	White Blood Cell
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index