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PHYTOCHEMICAL COMPOSITION, PHARMACOLOGICAL PROPERTIES, AND THERAPEUTIC PROSPECTS OF ZIZIPHORA SPECIES

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Annotation: This article analyzes the phytochemical composition, medicinal properties, and prospects for the use of Ziziphora spp. in traditional and modern medicine. Based on a review of scientific literature, the plant's chemical composition, including essential oils, thymol, pulegone, menthone, flavonoids, phenolic compounds, and other bioactive substances, was examined. These compounds possess antimicrobial, anti-inflammatory, antioxidant, antispasmodic, and antiseptic properties. Ziziphora has been widely used in traditional medicine for the treatment of common colds, respiratory tract diseases, digestive disorders, and inflammatory conditions. In modern medicine, it is considered a promising adjunctive remedy for the treatment of certain mild diseases. This article summarizes the phytochemical composition, pharmacological effects, and potential applications of Ziziphora in traditional and modern medicine based on scientific literature.
Keywords: Ziziphora spp., phytotherapy, essential oils flavonoids, pharmokological activity, bioactive compounds, medicine

KIYIKO'T (ZIZIPHORA)NING FITOKIMYOVIY TARKIBI, SHIFOBAXSH XUSUSIYATLARI, TABOBAT VA TIBBIYOTDA QO'LLANILISH ISTIQBOLLARI

Annotatsiya: Ushbu maqolada kiyiko't (Ziziphora spp.) ning fitokimyoviy tarkibi, shifobaxsh xususiyatlari hamda tabobat va tibbiyotda qo'llanilish istiqbollari tahlil qilindi. Ilmiy adabiyotlar tahlili asosida o'simlik tarkibidagi efir moylari, timol, pulegon, menton, flavonoidlar, fenol birikmalari va boshqa biologik faol moddalar o'rganildi. Ushbu moddalar antimikrob, yallig'lanishga qarshi, antioksidant, spazmolitik hamda antiseptik xususiyatlarga ega. Kiyiko't xalq tabobatida shamollash, nafas yo'llari kasalliklari, ovqat hazm qilish tizimi buzilishlari va yallig'lanish holatlarida keng qo'llaniladi. Zamonaviy tibbiyotda esa ayrim yengil kasalliklarni davolashda yordamchi vosita sifatida qo'llash istiqbolli hisoblanadi. Mazkur maqolada kiyiko'tning fitokimyoviy tarkibi, farmakologik ta'siri va tabobat hamda tibbiyotdagi qo'llanilish imkoniyatlari ilmiy adabiyotlar asosida umumlashtirildi.
Kalit so'zlar: Kiyiko't (Ziziphora spp.), fitoterapiya, efir moylari, flavonoidlar, farmakologik faollik, biologik faol moddalar, tibbiyot.

INTRODUCTION

Medicinal plants remain important sources of pharmacologically active molecules and continue to contribute to traditional health practices, food systems, and drug discovery. The genus Ziziphora L. belongs to the Lamiaceae family and includes aromatic annual or perennial herbs distributed across Southern and Eastern Europe, Central and Western Asia, the Middle East, and North Africa. Recent taxonomic syntheses describe approximately 31 taxa, although the accepted number can change as nomenclature is revised. Ziziphora clinopodioides, Ziziphora tenuior, Ziziphora persica, Ziziphora

capitata, Ziziphora hispanica, and several subspecies of Z. clinopodioides are the most frequently investigated taxa [1,2].

In Central Asia, including Uzbekistan, the aerial parts of Ziziphora species are used as herbal infusions, decoctions, seasonings, and household remedies. Ethnobotanical reports associate these preparations with cough, common cold, digestive discomfort, headache, fever, inflammation, and cardiovascular symptoms [4-6]. Such reports document cultural practice rather than clinical efficacy. They are nevertheless valuable for identifying research priorities and for understanding how plant material is prepared and consumed in the community.

The pharmacological interest in Ziziphora is linked to its chemically diverse volatile and nonvolatile fractions. Essential oils commonly contain oxygenated monoterpenes such as pulegone, menthone, isomenthone, 1,8-cineole, terpinen-4-ol, piperitone, thymol, and carvacrol. Nonvolatile extracts contain phenolic acids, caffeic acid derivatives, flavonoids, and triterpenes. A 2025 review catalogued 17 phenolic derivatives, 40 flavonoids, and 28 terpenoid derivatives that had been structurally characterized from the genus [1]. These constituents are biologically plausible contributors to antimicrobial, antioxidant, anti-inflammatory, smooth-muscle, and metabolic effects; however, the relative abundance of each compound varies substantially among species and growing environments.

Variation is a central problem for translation. The same botanical species may produce a pulegone-rich, cineole-rich, thymol-rich, or carvacrol-rich essential oil depending on geographic origin, climate, soil, harvest stage, plant organ, cultivation conditions, and analytical method [3,8-10]. Consequently, a result obtained with one extract cannot be generalized to all Ziziphora teas, oils, or commercial products. The extract type and chemical fingerprint must accompany any efficacy or safety claim.

The original Uzbek manuscript summarized the principal constituents and traditional uses of kiyiko't but did not include a reproducible review method, a separate Results section, or a critical appraisal of the evidence. The present article expands that material into a structured narrative review in IMRAD format. Its objectives are to describe the phytochemical profile of Ziziphora species, summarize representative pharmacological findings, examine toxicological concerns, and define the evidence required before medical or pediatric use can be recommended.

MATERIALS AND METHODS

Review Design and Scope - This work was designed as a structured narrative review rather than a systematic review or meta-analysis. A narrative design was selected because the available studies differ markedly in taxonomy, plant part, extraction method, analytical platform, biological model, dose expression, and outcome measure. The review focused on Ziziphora species and excluded similarly named but taxonomically distinct genera such as Ziziphus and Zataria.

Search Strategy and Eligibility - Literature was identified through PubMed, publisher databases, DOI records, and regulatory sources. Searches combined the term Ziziphora with species names and the terms phytochemistry, essential oil, flavonoid, phenolic, antimicrobial, antioxidant, anti-inflammatory, vasorelaxant, metabolic, toxicity, genotoxicity, pulegone, and pediatric. Publications from 1990 through September 2026 were considered, with earlier foundational compositional studies retained when they were repeatedly cited and analytically relevant.

Peer-reviewed studies were eligible when the plant taxon was identified, the investigated preparation was defined, and the analytical or pharmacological method was sufficiently described. Experimental studies, ethnobotanical studies, focused reviews, and authoritative safety documents were included. Duplicate reports, papers that did not distinguish Ziziphora from other genera, and claims lacking a traceable experimental basis were excluded from the core synthesis. Because the

purpose was critical synthesis rather than exhaustive enumeration, the most informative and verifiable studies were prioritized.

Data Extraction and Synthesis - For each source, the plant species, origin, plant part, preparation, analytical method, dominant constituents, biological model, principal finding, and evidence level were extracted. Quantitative values were reported only when they were directly available and interpretable. Findings were grouped into ethnomedicinal use, phytochemistry, antimicrobial and antioxidant activity, inflammation and cardiovascular activity, metabolic effects, and safety. No pooled effect estimate was calculated because of methodological heterogeneity.

Table 1 Review framework and eligibility criteria

Domain	Approach	Rationale
Information sources	PubMed; publisher databases; DOI records; regulatory documents	Combines biomedical indexing with primary publications and authoritative safety guidance
Time frame	1990 to September 2026 with selected earlier foundational reports	Captures modern analytical methods while retaining historically important compositional studies
Core search concepts	Ziziphora plus phytochemistry, essential oil, bioactivity, safety, toxicity, pulegone, and pediatric	Links taxonomy and preparation to biological and clinical relevance
Inclusion	Identified taxon defined preparation described method interpretable result	Reduces ambiguity caused by variable raw materials and extraction procedures
Exclusion	Ziziphus or Zataria studies duplicate records unsupported therapeutic claims	Prevents taxonomic confusion and overstatement
Synthesis	Structured narrative comparison without meta analysis	Assays doses units and models were too heterogeneous for valid pooling

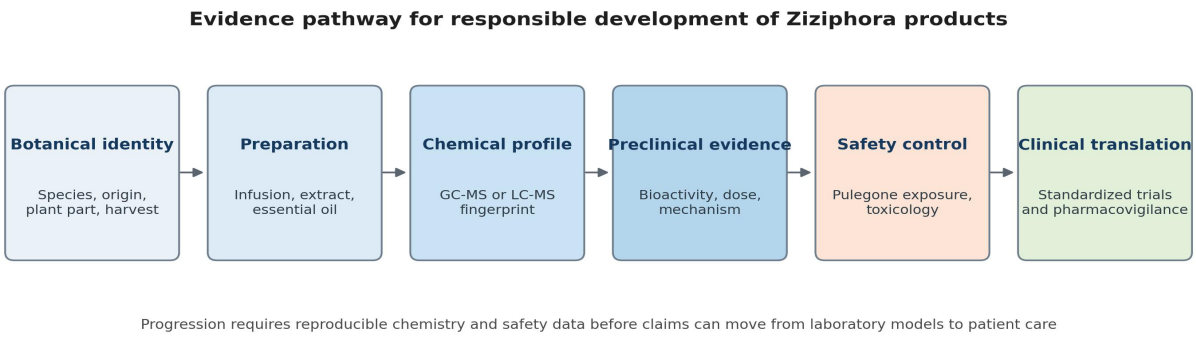


Figure 1 Evidence pathway for the development of standardized Ziziphora products. The diagram distinguishes laboratory plausibility from the additional quality and safety steps required before clinical use.

RESULTS

Botanical Distribution and Ethnomedicinal Context - Ziziphora species are small aromatic herbs with glandular trichomes that synthesize and store volatile oil. The aerial parts, especially leaves and flowering shoots, are the most common medicinal and culinary materials. Z. clinopodioides is a perennial species, whereas several other members of the genus are annual. In Uzbekistan and neighboring Central Asian regions, preparations have included infusions, decoctions, and tinctures. Reported uses include respiratory discomfort, digestive complaints, wound care, headache, dizziness, and cardiovascular symptoms [1,4-6].

The correspondence between traditional use and experimental evidence is uneven. Antimicrobial and antioxidant assays broadly support biological activity, and vasorelaxant experiments offer a possible mechanism for some traditional cardiovascular use. By contrast, traditional indications such as common cold, cough, diarrhea, or pediatric digestive disorders have not been established through controlled clinical trials of standardized Ziziphora preparations. Ethnomedicinal use should therefore be presented as a source of hypotheses rather than proof of therapeutic benefit.

Table 2 Selected Ziziphora taxa and reported traditional use

Taxon	Region	Common preparation	Reported traditional context	Source
Z. clinopodioides	Central and Western Asia, Middle East	Infusion of leaves or aerial parts	Cold and cough, digestive discomfort, inflammation, headache, cardiovascular symptoms	[1,2]
Z. clinopodioides subsp. bungeana	Kyrgyzstan and Uzbekistan	Decoction of aerial parts	Respiratory distress, dizziness, cardiovascular symptoms	[1,6]
Z. pedicellata	Uzbekistan	Tincture or decoction of aerial parts	Diuretic and wound-care use, blood-pressure-related use	[1]

Taxon	Region	Common preparation	Reported traditional context	Source
Z. tenuior	Türkiye and Iran	Infusion or external decoction	Cold and flu, digestive complaints, wound and burn care	[1,2]
Z. persica	Iran	Leaf infusion or decoction	Abdominal discomfort, flatulence, dyspepsia, fever	[1]

Phytochemical Composition

The essential-oil fraction is the best studied component of the genus. Oxygenated monoterpenes predominate in many samples, but no single chemical profile defines every Ziziphora preparation. Pulegone often appears as a major constituent and has been reported at approximately 7.9% to more than 70% in selected samples. Other profiles are dominated by 1,8-cineole, carvacrol, thymol, terpinen-4-ol, alpha-terpineol, or caryophyllene derivatives [1,3,7-10]. The large range is not analytical noise alone; it reflects genuine chemotypic and environmental variability.

A 2026 study of Z. clinopodioides collected in Türkiye identified 98.3% of the essential oil and found oxygenated monoterpenes to be dominant. The leading compounds were 1,8-cineole at 28.2%, terpinen-4-ol at 12.0%, and pulegone at 7.9% [3]. In contrast, an Iranian sample reported by Shahbazi contained carvacrol at 64.2% and thymol at 19.2%, while another Iranian sample contained pulegone at 44.5% and terpineol at 14.5% [8,9]. These differences are clinically important because efficacy, organoleptic properties, and toxicological risk depend on the actual composition rather than the botanical name alone.

Nonvolatile constituents broaden the pharmacological profile. Reported phenolic compounds include rosmarinic acid, caffeic acid derivatives, protocatechuic acid, and p-coumarate derivatives. Flavonoids include apigenin, luteolin, acacetin, chrysin, rutin, hyperoside, baicalein, kaempferol derivatives, and multiple glycosides. Triterpenes include ursolic acid, oleanolic acid, betulinic acid, and related compounds [1,6,14]. Solvent polarity strongly affects which constituents are recovered: water and methanol favor many polar phenolics, whereas hydrodistillation concentrates volatile terpenoids.

Table 3 Representative phytochemical profiles of Ziziphora preparations

Species and origin	Preparation and method	Dominant or notable constituents	Interpretation	Source
Z. clinopodioides, Türkiye, 2026	Essential oil, GC-MS	1,8-cineole 28.2%; terpinen-4-ol 12.0%; pulegone 7.9%	Cineole-dominant oxygenated-monoterpene profile	[3]
Z. clinopodioides, Iran	Essential oil, GC-MS	Carvacrol 64.2%; thymol 19.2%; p-cymene 4.8%; gamma-terpinene 4.6%	Phenolic-monoterpene-rich chemotype	[8]

Species and origin	Preparation and method	Dominant or notable constituents	Interpretation	Source
Z. clinopodioides, Iran	Hydrodistilled essential oil, GC-MS	Pulegone 44.5%; terpineol 14.5%; methyl acetate 10.9%; iso-neomenthol 7.1%	Pulegone-rich profile with menthane derivatives	[9]
Z. clinopodioides and Z. tenuior, cultivated in Iran	Flowering aerial-part essential oils, GC-MS	Pulegone 70.4% and menthone 11.5% in Z. clinopodioides; pulegone 55.1% and limonene 8.2% in Z. tenuior	Species and cultivation still produced distinct quantitative profiles	[10]
Z. clinopodioides subsp. bungeana	Fractionation and structure elucidation	Betulinic acid, ursolic acid, oleanolic acid, 11-oxoursolic acid, and a monoterpene diperoxy dimer	Nonvolatile triterpenes may contribute to metabolic activity	[14]
Z. tenuior leaves	Methanol and dichloromethane extracts, GC-MS	Pulegone was the leading component in both fractions	Solvent choice changed both composition and antioxidant activity	[15]

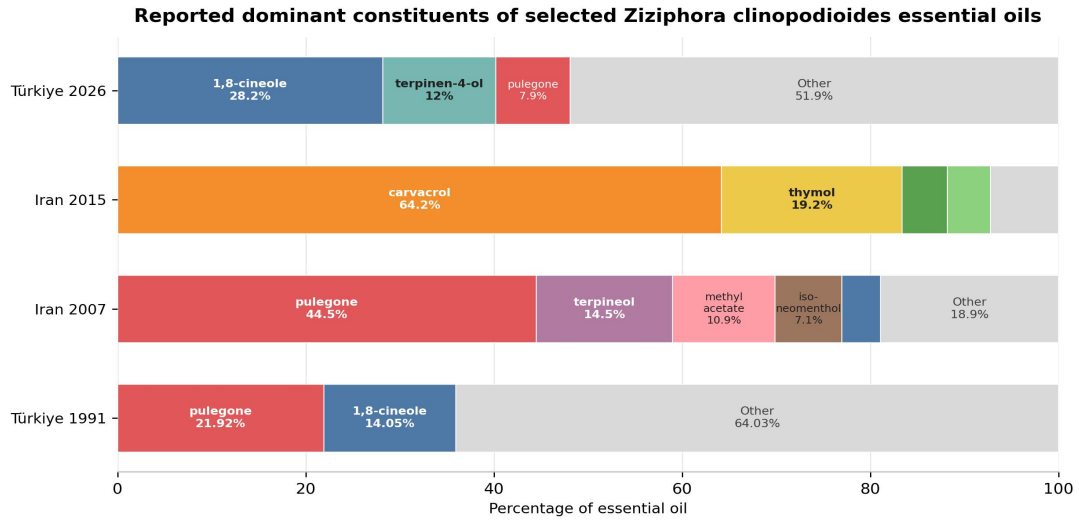


Figure 2 Dominant constituents reported for selected Ziziphora clinopodioides essential oils [3,8,9]. The residual segment represents all other constituents in each analysis. The figure demonstrates why species identification alone is insufficient for standardization.

Antimicrobial and Antioxidant Evidence

Antimicrobial activity is the most consistently investigated property of Ziziphora. The essential oil and methanol extract of Z. clinopodioides were tested against 52 Gram-positive and Gram-negative bacterial strains. The oil contained pulegone at 31.86%, 1,8-cineole at 12.21%, limonene at 10.48%, and menthol at 9.13%, and both preparations produced broad in vitro inhibition [7]. In another study, Z. clinopodioides essential oil showed minimal inhibitory concentrations from 0.003% to

0.067% against selected bacterial strains and fungicidal activity above 1 microliter per milliliter against two dermatophytes [9]. These results demonstrate biological activity, but assay conditions and units differ across studies, limiting direct comparison.

Comparative work on cultivated Z. clinopodioides and Z. tenuior found inhibition zones of approximately 12 to 19 mm against selected foodborne bacteria. Z. clinopodioides showed antioxidant activity in the DPPH assay with an IC50 of 111.4 ± 1.2 µg/mL, while Z. tenuior showed an IC50 of 147.2 ± 1.3 µg/mL [10]. A separate Z. tenuior study showed that growth stage altered total phenolics, essential-oil composition, and radical-scavenging activity [20]. The antioxidant effect of a complex extract cannot therefore be attributed to one compound without activity-guided fractionation.

Mechanistic cell experiments support an antioxidant signal. A flavonoid-rich fraction of Z. clinopodioides reduced hydrogen-peroxide-induced injury in human umbilical-vein endothelial cells, decreased malondialdehyde and lactate dehydrogenase, increased antioxidant enzyme activity, and altered apoptosis-related signaling [11]. This is useful mechanistic evidence, but it remains an in vitro model and does not establish clinical cardiovascular protection.

Inflammatory, Cardiovascular, and Metabolic Evidence

Anti-inflammatory activity has been demonstrated in animal models. Z. clinopodioides extracts reduced paw edema in carrageenan, histamine, and serotonin models and reduced ear edema in a xylene model. In a chronic adjuvant arthritis model, treatment reduced inflammatory progression and improved histopathological features [12]. Z. tenuior extract also reduced inflammatory and apoptosis-related gene expression in liver and lung tissue in a rat model of chlorpyrifos toxicity [17]. Although these findings are coherent with traditional anti-inflammatory use, they do not define a safe or effective dose for humans.

Cardiovascular evidence includes ex vivo vasorelaxation and animal studies. A dichloromethane extract of Z. clinopodioides relaxed phenylephrine- and potassium-chloride-precontracted rat aortic rings with EC50 values of 0.27 ± 0.03 and 0.34 ± 0.04 g/L, respectively. The effect was endothelium independent and involved calcium handling and voltage-dependent potassium channels [13]. Flavonoid fractions have also shown anti-atherosclerotic effects in rats, but the doses and complex mechanisms require independent replication before clinical interpretation [1].

Table 4 Representative pharmacological evidence and its interpretation

Preparation	Model	Key finding	Evidence level and limitation	source
Z. clinopodioides essential oil and methanol extract	Broth microdilution against 52 bacterial strains	Broad in vitro antibacterial activity; composition dominated by pulegone and other monoterpenes	In vitro; heterogeneous organisms and no human outcome	[7]
Z. clinopodioides and Z. tenuior essential oils	Foodborne bacteria and DPPH assay	Inhibition zones about 12 to 19 mm; DPPH IC50 values of 111.4 and 147.2 µg/mL	In vitro; results depend on oil chemistry and assay	[10]

Preparation	Model	Key finding	Evidence level and limitation	ource
Z. clinopodioides flavonoids	Hydrogen-peroxide-injured HUVEC cells	Lower oxidative injury markers and apoptosis with higher antioxidant enzyme activity	Mechanistic cell evidence; no pharmacokinetic data	[11]
Z. clinopodioides extracts	Acute edema and chronic arthritis models in rodents	Reduced edema, inflammatory progression, and histopathological injury	Animal evidence; dose translation uncertain	[12]
Z. clinopodioides dichloromethane extract	Isolated rat thoracic aorta	Endothelium-independent relaxation with EC50 0.27 and 0.34 g per L	Ex vivo evidence; cannot predict clinical blood-pressure effect	[13]
Triterpenes from Z. clinopodioides subsp. bungeana	Alpha-glucosidase and GLUT4 assays	Betulinic acid IC50 45.3 micromolar versus acarbose 264.7 micromolar	Compound-level in vitro signal; not evidence for crude tea or extract	[14]
Z. clinopodioides essential oil and extracts	Enzyme-inhibition assays	Modest alpha-amylase and cholinesterase inhibition below reference drugs	Preliminary in vitro evidence	[3]

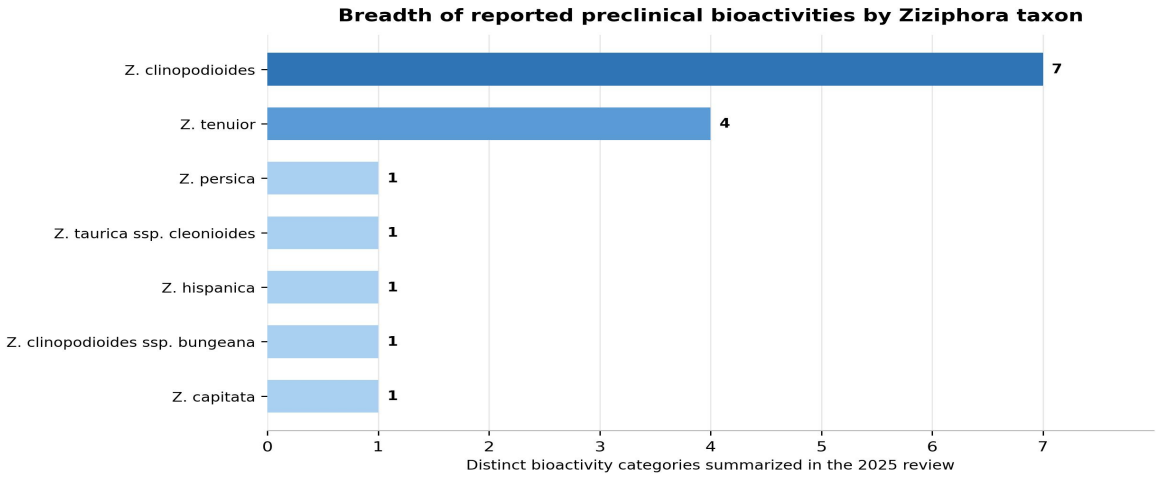


Figure 3 Breadth of preclinical bioactivity categories summarized by taxon in the 2025 review [1]. Counts represent distinct categories, not numbers of studies, effect sizes, or clinical efficacy.

Metabolic investigations are emerging. In the 2026 Z. clinopodioides study, essential oil inhibited alpha-amylase by 29.3%, whereas the methanol and aqueous extracts inhibited it by 20.89% and 11.92%; all were weaker than acarbose under the reported assay conditions. Methanol extract produced only moderate acetylcholinesterase and butyrylcholinesterase inhibition compared with donepezil [3]. Conversely, isolated triterpenes from Z. clinopodioides subsp. bungeana showed stronger alpha-glucosidase inhibition than acarbose in vitro, with betulinic acid producing an IC50 of 45.3 micromolar compared with 264.7 micromolar for acarbose [14]. Isolated-enzyme potency is a discovery signal, not evidence that the crude plant preparation treats diabetes.

Safety Findings and Pediatric Relevance

The widespread culinary or traditional use of a plant does not establish the safety of concentrated extracts or essential oils. In an in vitro safety study of Z. clinopodioides ethanolic extract, human lymphocyte viability declined in a dose-dependent manner at 1 to 10 mg/mL. The comet assay showed increasing DNA damage at 5 and 10 mg/mL, whereas the Ames test did not show mutagenicity in the tested Salmonella strains [16]. The result does not prove that customary infusions cause genotoxicity, but it demonstrates that preparation and concentration matter and that a high-dose extract should not be treated as equivalent to food use.

Pulegone requires particular attention because it is metabolized to reactive intermediates, including menthofuran, and high experimental exposures can damage the liver and kidney. The European Medicines Agency recommends keeping exposure to pulegone and menthofuran as low as practically achievable and applying product-specific thresholds. Its 2016 statement proposed an acceptable combined exposure of 0.75 mg/kg body weight per day for herbal medicinal products, with weight-based adjustment for children; these limits were derived largely from nonclinical toxicology and are not a dosing recommendation for Ziziphora [18,19].

No pediatric pharmacokinetic study, dose-ranging trial, randomized efficacy trial, or prospective safety study of a chemically standardized Ziziphora product was identified in the reviewed literature. For this reason, the plant cannot currently be recommended as a pediatric treatment for respiratory, inflammatory, or gastrointestinal disease. If a future pediatric product is developed, it should include authenticated raw material, a validated chemical fingerprint, quantitative limits for pulegone and menthofuran, age-appropriate formulation studies, toxicology, interaction assessment, and staged clinical evaluation.

Table 5 Evidence gaps and priorities for clinical translation

Gap	Why it matters	Minimum research requirement
Taxonomic and chemical variability	Different chemotypes may produce different efficacy and toxicity	Voucher specimen, origin, harvest stage, extraction yield, and GC-MS or LC-MS fingerprint
Unstandardized preparations	Tea, tincture, solvent extract, and essential oil are not interchangeable	Defined drug-extract ratio, solvent, marker compounds, and batch-acceptance limits
Pulegone and menthofuran exposure	Potential liver and kidney toxicity depends on actual dose	Validated quantification, impurity control, exposure calculation, and repeat-dose toxicology

Gap	Why it matters	Minimum research requirement
Predominantly preclinical efficacy	Cell and animal effects may not translate to patient benefit	Dose-finding followed by controlled human trials with prespecified outcomes
No pediatric clinical evidence	Children differ in body mass, metabolism, and susceptibility	Adult safety first, juvenile toxicology when justified, pediatric pharmacokinetics, and ethics-approved trials
Limited interaction data	Essential oils and polyphenols may alter enzymes or medicines	In vitro interaction screening followed by clinically relevant assessment

DISCUSSION

Interpretation of the Evidence

The reviewed literature consistently shows that Ziziphora species contain biologically active volatile and nonvolatile constituents. Antimicrobial, antioxidant, anti-inflammatory, vasorelaxant, immunomodulatory, and enzyme-inhibitory findings are supported by multiple experimental models. The strongest conclusion is therefore that the genus is a credible source for natural-product research. A stronger conclusion that Ziziphora preparations are clinically effective would exceed the evidence.

The gap between laboratory activity and therapeutic use is widened by chemical variability. For example, one Z. clinopodioides oil was dominated by carvacrol and thymol, another by pulegone, and a recent Turkish sample by 1,8-cineole and terpinen-4-ol [3,8,9]. Each profile is likely to differ in antimicrobial spectrum, odor, absorption, metabolism, and toxicological burden. Publications should therefore report the chemical fingerprint of the exact material tested, and clinical development should use a fixed, reproducible preparation.

The evidence also cautions against describing all observed effects as medicinal benefits. Cytotoxicity can be desirable in an anticancer screening assay but undesirable in normal human cells. Antimicrobial inhibition in a culture plate does not show that an oral tea reaches an effective concentration at an infection site. Radical-scavenging assays do not establish prevention of clinical oxidative-stress disorders. These distinctions are essential for scientifically accurate communication and safe patient counseling.

Translational and Standardization Priorities

A rational development program should begin with botanical authentication and conservation-aware sourcing. The plant part, location, altitude, soil, harvest time, drying conditions, and storage duration should be recorded. Extracts should then be standardized using chromatographic fingerprints and quantitative markers selected for both activity and safety. For pulegone-rich materials, the content of pulegone and menthofuran should be measured in the final daily dose rather than reported only as a percentage of essential oil.

The next step is formulation-specific pharmacology and toxicology. Studies should define absorption, metabolism, tissue exposure, and interaction potential. Repeated-dose toxicity, genotoxicity, reproductive toxicity when relevant, and local tolerability should be evaluated using internationally accepted methods. Only after a reproducible safety margin is established should exploratory clinical trials assess tolerability, pharmacokinetics, and a narrowly defined indication.

For pediatric development, evidence from adults cannot replace direct consideration of age, body weight, organ maturation, formulation acceptability, and co-medication. Initial pediatric

studies would need a compelling clinical rationale, a standardized preparation with low and controlled toxicological constituents, and ethics oversight. Until such data exist, pediatric references to Ziziphora should remain limited to research prospects and safety cautions rather than treatment recommendations.

Limitations

This review is structured but not systematic. It did not attempt exhaustive multilingual retrieval, formal risk-of-bias scoring, or meta-analysis. Some older studies used taxonomic names that have since been revised, and several reports did not provide a full chemical fingerprint. The pharmacological studies used different extracts, doses, organisms, cell lines, and outcome measures, which prevents quantitative pooling. Negative publication bias is also possible because inactive extracts may be less likely to be reported.

The safety analysis relies on a limited number of Ziziphora-specific experiments supplemented by toxicological evidence on pulegone and menthofuran from other mint-derived preparations. Those data are relevant to chemical hazard assessment but do not directly measure the risk of every traditional Ziziphora infusion. The practical implication is not that all use is unsafe; it is that safety conclusions must be preparation-specific and exposure-based.

Conclusion

Ziziphora species contain essential oils, phenolic acids, flavonoids, and triterpenes with reproducible biological activity in laboratory and animal models. The best-supported experimental signals are antimicrobial, antioxidant, anti-inflammatory, vasorelaxant, and metabolic-enzyme effects. Their translational value is limited by marked chemotypic variation, inconsistent preparation methods, scarce pharmacokinetic information, and the absence of controlled human and pediatric trials. Pulegone-rich preparations also require quantitative toxicological control. Current evidence supports further pharmacognostic, pharmaceutical, and preclinical development, but it does not support routine therapeutic use or pediatric dosing. Future research should prioritize authenticated plant material, batch standardization, exposure-based safety assessment, and indication-specific clinical trials.

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