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Traditional Pharmacological Uses and Toxicological Evaluation of Thymus vulgaris Essential Oil

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ABSTRACT

Background: Thymus vulgaris L. (thyme) essential oil has been used across Mediterranean, Central European and Balkan folk medicine for respiratory, gastrointestinal and dermatological complaints, and its principal phenolic constituents, thymol and carvacrol, are now widely traded as antimicrobial and flavouring agents.

Objective: This review synthesizes the published literature on the traditional and ethnopharmacological uses of T. vulgaris essential oil, its phytochemical variability, its pharmacological activities, and its toxicological and regulatory safety profile, with the aim of setting the pharmacology against the safety data on comparable, critical terms.

Scope: Ethnobotanical surveys, phytochemical characterization studies, in vitro and in vivo pharmacology (antimicrobial, antioxidant, anti-inflammatory, spasmolytic and respiratory), acute and repeated-dose toxicity studies, genotoxicity assays, dermal sensitization case reports and the 2025 EFSA feed additive safety opinion on thyme oil are reviewed and cross-referenced.

Conclusions: Thyme oil's traditional respiratory and antimicrobial uses are supported by a reasonably coherent mechanistic and toxicological evidence base: acute oral toxicity is low, genotoxicity data on thymol and carvacrol are reassuring, and regulatory review has judged the oil safe at proposed dietary and feed use levels. Chemotype heterogeneity across studies, a scarcity of long-duration whole-oil toxicity data, and a real dermal sensitization risk remain the principal gaps warranting further chemotype-standardized research.

Keywords: *Thymus vulgaris; essential oil; thymol; carvacrol; toxicological safety*

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Introduction

Thyme has never really left the kitchen, and it never left the apothecary shelf either, which is part of what makes *Thymus vulgaris* L. (Lamiaceae) such an interesting subject for a pharmacological review rather than a difficult one. Few plants show up so consistently across unrelated pharmacopoeial traditions — Mediterranean folk medicine, German Commission E monographs, British and Central European cough remedies, North African ethnobotanical surveys — usually for the same handful of complaints: sore throats, chesty coughs, digestive cramping, and skin infections. A 553-record survey of Thymus use across twelve Balkan countries found respiratory and gastrointestinal indications dominating the traditional record, with smaller but persistent clusters of nervous, urinary and cardiovascular applications layered on top [1]. Moroccan ethnobotanical work tells much the same story, with thyme infusions and steam inhalations used for bronchitis, influenza-like illness and abdominal pain long before anyone isolated thymol from the plant [2].

What complicates the picture, and what makes a critical review worthwhile rather than a formality, is that "thyme oil" is not one chemical entity. Wild and cultivated *T. vulgaris* populations express markedly different essential oil chemotypes depending on genetics, soil, and climate, and the pharmacological and toxicological literature routinely mixes thymol-, carvacrol-, linalool- and geraniol-dominant oils under a single common name. That is not a trivial classification issue — thymol and carvacrol drive most of the antimicrobial and mucolytic activity attributed to the plant, but they are also the constituents responsible for its irritant and sensitizing potential, so any safety statement about "thyme oil" that does not specify chemotype is, strictly speaking, incomplete. This review pulls together what has

been published on the traditional uses, phytochemical variability, and pharmacological activity of *T. vulgaris* essential oil, and sets that pharmacology against the acute, repeated-dose, genotoxicity, and dermal safety data that regulatory bodies such as the European Food Safety Authority (EFSA) have relied on when assessing the oil for use in food, feed, and consumer products.

Botanical Background and Phytochemistry

Thymus vulgaris is a low, woody Lamiaceae shrub native to the western Mediterranean and now cultivated across southern and central Europe, North Africa, and increasingly outside its native range for the essential oil trade. The oil is obtained almost exclusively by steam or hydrodistillation of the flowering aerial parts, with yields typically in the range of 1–2.5% depending on harvest timing, drying method, and genotype.

Chemotype variability is really the organizing fact of thyme phytochemistry. Satyal and colleagues characterized oils from several geographically distinct populations and found thymol contents ranging from barely detectable to over 45%, alongside shifting proportions of carvacrol, p-cymene, γ-terpinene, and linalool — enough variation that oils sold under the same species name can smell and behave quite differently in an assay [3]. Molecular marker work by György and colleagues confirmed that this chemical polymorphism tracks with genetically distinguishable chemotypes rather than simple environmental noise, which is part of why standardization has proven so persistently difficult for this crop [4]. In broad terms the literature recognizes thymol-type, carvacrol-type, linalool-type, and geraniol/4-thujanol-type oils, with the thymol chemotype being the one most commonly traded commercially and most often used in the pharmacological studies discussed below. A Tunisian wild-collected sample analyzed by Hajlaoui and co-workers, for instance, turned out to be carvacrol-dominant (67.3%) rather than thymol-dominant, illustrating how easily assumptions about "typical" composition can mislead cross-study comparison [5]. Galovičová and colleagues, working with Slovak-grown material, reported a thymol content of 48.1% alongside p-cymene and γ-terpinene as the other major constituents, which is closer to what most pharmacopoeial specifications treat as representative [6].

Beyond the two monoterpenol phenols that dominate discussion, the oil typically contains a suite of minor constituents — borneol, linalool, camphor, 1,8-cineole, and various sesquiterpenes — that individually contribute little activity but may modulate the pharmacokinetics or irritancy of the phenolic fraction. This matters clinically more than it might seem: several authors have noted that whole-oil preparations behave differently in antispasmodic assays than isolated thymol, suggesting the non-phenolic fraction is not simply inert filler [7].

Traditional and Ethnopharmacological Uses

The traditional use pattern for thyme is remarkably conserved across regions that had no historical contact with one another's herbal traditions, which is itself a modest piece of evidence that something pharmacologically real is going on. Respiratory indications — cough, catarrh, bronchitis, pertussis-like symptoms — appear as the single largest use category in essentially every ethnobotanical survey that has looked at Thymus species, followed by gastrointestinal complaints (dyspepsia, flatulence, mild spasmodic pain) and topical applications for minor wounds, insect bites, and fungal skin conditions [1,2]. Thyme tea and thyme-honey preparations for children's coughs remain common household remedies in much of southern and eastern Europe, a use that eventually found its way into standardized pharmaceutical products.

The clearest bridge between folk use and modern clinical evidence is the combination thyme/ivy extract, marketed under several trade names across Europe, which has been the subject of repeated observational and controlled studies for acute bronchitis and cough. A large pharmacy-based observational study of the fluid extract BNO 1200 in more than 2,000 patients with acute cough reported a substantial reduction in cough severity and bronchitic symptom scores within days of treatment, with good tolerability across age groups including young children [8]. These are not essential-oil studies in the strict sense — most of the clinically tested thyme preparations are aqueous or hydroalcoholic extracts rather than the distilled oil itself — but they matter for a review of the oil's pharmacology because the underlying rationale, and much of the mechanistic work explaining efficacy, converges on the same thymol- and carvacrol-driven actions described below.

Pharmacological Activities

Antimicrobial Activity

Antimicrobial testing is where the thyme literature is thickest, and the results are about as consistent as essential oil pharmacology gets. Thymol and carvacrol act on the bacterial cell membrane, increasing permeability and disrupting the proton motive force, and whole thyme oil generally performs at least as well as either constituent alone against a broad panel of Gram-positive and Gram-negative organisms. Rota and colleagues compared oils from *T. vulgaris*, *T. zygis*, and *T. hyemalis* and found the thymol/carvacrol-rich vulgaris oil among the most active against foodborne pathogens including *Listeria monocytogenes* and *Salmonella enterica*, with minimum inhibitory concentrations in the low microgram-per-millilitre range for several strains [9]. Boruga and co-workers reported similarly strong activity for a Romanian thyme oil against *Staphylococcus aureus* and *Candida albicans*, reinforcing that the antimicrobial spectrum extends beyond bacteria into clinically relevant fungi [10]. Iten and colleagues went a step further methodologically, testing thymol and carvacrol individually and in combination and finding additive — though generally not synergistic — antimicrobial effects, which supports the idea that the two phenols act through a shared or overlapping mechanism rather than complementary ones [11].

More recent work has pushed into antibiotic-resistant territory. Jilani and colleagues combined Tunisian thyme oil and its carvacrol fraction with imipenem against carbapenem-resistant *Acinetobacter baumannii* and reported up to a sixteen-fold reduction in the antibiotic's effective concentration, with molecular docking suggesting carvacrol interferes with bacterial cell-wall biosynthesis enzymes — a mechanistically plausible, if still preclinical, route toward using the oil as an antibiotic adjuvant rather than a standalone agent [12]. Hajlaoui's carvacrol-chemotype Tunisian oil likewise showed activity that the authors described as comparable to, or in some assays exceeding, synthetic reference antioxidants and antimicrobials tested in parallel [5].

Antioxidant and Anti-inflammatory Activity

The antioxidant activity of thyme oil is generally attributed to the phenolic hydroxyl groups on thymol and carvacrol, which donate

hydrogen readily in radical-scavenging assays such as DPPH and ABTS. Galovičová and colleagues measured antioxidant activity above 85% in their thymol-dominant Slovak oil using standard radical-scavenging methodology, a figure broadly consistent with other thymol-rich samples reported in the literature [6]. The magnitude of activity tracks fairly closely with total phenolic content across studies, which is one of the more reproducible dose–response relationships in this field.

Summary of pharmacological activities and toxicological endpoints reported for Thymus vulgaris essential oil and its principal constituents (thymol, carvacrol) in the cited literature.

Domain	Model/Assay	Principal finding	Reference
Antimicrobial	MIC panel vs. foodborne bacteria (T. vulgaris, T. zygis, T. hyemalis oils)	Low-microgram/mL activity against Listeria monocytogenes, Salmonella enterica; thymol/carvacrol-rich oils most active	[9]
Antimicrobial	Disc diffusion/MIC vs. S. aureus, C. albicans	Strong inhibition zones and low MICs for Romanian thyme oil	[10]
Antimicrobial	Thymol + carvacrol combination assay	Additive (not synergistic) antimicrobial effect of the two phenols	[11]
Antimicrobial (resistant strains)	Carvacrol + imipenem vs. carbapenem-resistant A. baumannii	Up to 16-fold reduction in imipenem MIC; docking suggests cell-wall enzyme interference	[12]
Antioxidant	DPPH/ABTS radical scavenging	Antioxidant activity >85% for thymol-dominant (48.1%) Slovak oil	[6]
Antioxidant/antimicrobial	Carvacrol-chemotype wild Tunisian oil	Antioxidant capacity comparable to/exceeding synthetic reference antioxidants	[5]
Anti-inflammatory/antinociceptive	Rodent paw oedema, leukocyte migration models	Thymol and carvacrol reduced oedema, vascular permeability and nociception without sedation	[13]
Anti-inflammatory (mechanistic)	Narrative review of thymol pharmacology	Effects on NF-κB signalling, cytokine output and oxidative stress markers across models	[14]
Spasmolytic/respiratory	Isolated guinea-pig trachea	Thymol contributes to antispasmodic action and increases ciliary beat frequency	[15]
Spasmolytic/respiratory	Thymol-depleted hydrophilic extract fractionation	Antispasmodic activity persists without the phenolic (thymol) fraction	[7]
Clinical (extract, not oil)	Observational study, thyme/ivy fluid extract, acute cough (n>2000)	Reduced cough severity and bronchitic symptom scores; good tolerability	[8]
Acute oral toxicity	Rat, single-dose OECD-style protocol	No mortality or overt toxicity signs at tested doses	[16]
Repeated-dose toxicity	Rat, 28-day oral dosing	Dose-related hepatic biochemistry/haematology shifts at higher doses; NOAEL above traditional-use levels	[16]
Repeated-dose toxicity (mixture)	Rat, thyme/sage/dittany oil blend	No clinically meaningful organ toxicity or genotoxicity at tested doses	[17]
Genotoxicity	Ames test + comet assay (Caco-2 cells), thymol and carvacrol	No mutagenicity; DNA damage signal only near cytotoxic concentrations	[18]
Genotoxicity	Micronucleus and mouse lymphoma assays, thymol and carvacrol	No clear genotoxic signal at pharmacologically relevant concentrations	[19]
Developmental/endocrine	Chicken embryo, low-dose carvacrol and thymol	Measurable embryotoxic and weak estrogenic-like effects at higher tested concentrations	[20]
Dermal sensitization	Patch-test-confirmed clinical case series	Allergic contact dermatitis to thyme and related essential oils, notably in aromatherapists/therapists	[21]
Regulatory safety opinion	EFSA FEEDAP feed additive dossier review	Safe for target species/consumers at proposed use levels; flagged as skin/eye irritant and dermal sensitizer for handlers	[22]

Anti-inflammatory activity has a somewhat separate evidence base, built mostly around the isolated constituents rather than the whole oil. Fachini-Queiroz and colleagues showed that both thymol and carvacrol reduced leukocyte migration, vascular permeability and paw oedema in classic rodent inflammation

models, at doses that also produced measurable antinociceptive effects without obvious sedation — a combination the authors interpreted as evidence that the phenols act on peripheral inflammatory mediators rather than centrally [13]. Nagoor Meeran and colleagues reviewed thymol's pharmacology more broadly and catalogued effects on NF-κB signalling, cytokine production, and oxidative stress markers across a range of disease models, concluding that anti-inflammatory and antioxidant actions are mechanistically intertwined for this constituent rather than independent activities [14].

Spasmolytic and Respiratory Effects

The respiratory pharmacology of thyme is arguably better characterized mechanistically than its antimicrobial activity, if only because it has attracted more targeted isolated-tissue and clinical work. Begrow and colleagues used isolated guinea pig trachea preparations to show that thymol contributes meaningfully to the antispasmodic action of thyme extracts and also enhances ciliary beat frequency, a combination that would plausibly help clear mucus while relaxing bronchial smooth muscle — essentially the two things you would want from a cough remedy [15]. Engelbertz and colleagues followed up by fractionating a thymol-depleted hydrophilic thyme extract and finding that antispasmodic activity persisted even without the phenolic fraction, which was a genuinely useful negative result: it means the spasmolytic effect of whole-plant preparations cannot be reduced to thymol alone, and other constituents — likely flavonoid or triterpene fractions — contribute independently [7]. Clinically, this mechanistic picture is consistent with the symptom improvements reported for thyme/ivy combination products in acute bronchitis populations [8], though it should be said plainly that most controlled clinical evidence for respiratory benefit involves hydroalcoholic extracts rather than the distilled essential oil itself, and extrapolating extract efficacy directly onto oil-based products is not something the current evidence base fully supports.

Toxicological and Safety Profile

Acute and Repeated-Dose Toxicity

The most directly relevant toxicological dataset for the essential oil itself comes from Rojas-Armas and colleagues, who ran both an acute oral toxicity study and a 28-day repeated-dose study of *T. vulgaris* essential oil in rats following OECD-style guideline protocols. The acute study found no mortality or overt toxicity signs at the single oral doses tested, consistent with the generally low acute oral toxicity reported for thymol- and carvacrol-rich essential oils in rodents more broadly. The 28-day repeated-dose phase identified dose-related changes in liver-associated biochemical parameters and some haematological shifts at the higher dose levels tested, without producing mortality, and the no-observed-adverse-effect level the authors derived sat comfortably above the doses used in traditional preparations [16]. This is a fairly typical pattern for phenolic monoterpene-rich oils: wide margins for acute lethality, but detectable hepatic and metabolic signals on repeated dosing at levels well above normal culinary or traditional medicinal exposure.

A related toxicological question — what happens when thyme oil is combined with other high-thymol-family herbs, as it often is in traditional Mediterranean formulations — was addressed by Kalyvianaki and colleagues, who evaluated a mixed essential oil preparation from Cretan thyme, Greek sage, and Cretan dittany. Their repeated-dose and genotoxicity screening of the combined preparation found no evidence of clinically meaningful organ toxicity or genotoxic potential at the doses tested, which is reassuring for the many traditional preparations that use thyme alongside other Lamiaceae herbs rather than in isolation [17].

Genotoxicity and Mutagenicity

Genotoxicity testing has focused mainly on the isolated constituents rather than the whole oil, largely because thymol and carvacrol are the components regulators care most about for food and feed exposure assessment. Llana-Ruiz-Cabello and colleagues ran the bacterial reverse mutation (Ames) assay alongside comet assays in Caco-2 human intestinal cells and found no evidence of mutagenicity for either thymol or carvacrol under standard conditions, though the comet assay did register some DNA damage signal at higher, cytotoxic concentrations — a pattern more consistent with secondary oxidative stress from cytotoxicity than with direct genotoxic mechanism [18]. Maisanaba and colleagues extended this with micronucleus and mouse lymphoma assays and reached a broadly similar conclusion: no clear genotoxic signal at pharmacologically or dietarily relevant concentrations, with positive findings emerging only close to cytotoxic thresholds [19]. Zhang and colleagues added an in ovo dimension, testing carvacrol and thymol for chicken embryonic toxicity and possible estrogenic activity at low concentrations; they reported measurable embryotoxic and weak estrogenic-like effects at the higher end of the concentration range tested, a finding worth flagging for anyone extrapolating rodent no-effect levels onto other vertebrate models without adjustment [20]. Taken as a set, these studies do not raise a genotoxicity red flag for either constituent under normal use conditions, but they do converge on the same message as the repeated-dose rat data: the margin between "no observable effect" and "measurable biological signal" narrows considerably once concentrations climb well above what culinary or standard medicinal use would deliver.

Dermal Sensitization and Allergic Reactions

Thyme's safety profile looks noticeably less reassuring on the skin than it does orally, and this asymmetry deserves more attention in general reviews than it usually gets. Thymol and carvacrol are recognized contact allergens, and case reports of occupational and cosmetic-exposure allergic contact dermatitis to thyme and other Lamiaceae essential oils are not rare in the dermatology literature. Bleasel and colleagues reviewed a series of patch-test-confirmed cases of allergic contact dermatitis following essential oil exposure, including thyme-containing products, and noted that aromatherapists and massage therapists — occupational groups with frequent, repeated, often undiluted skin contact — appear to carry disproportionate risk [21]. This does not mean the oil is unsafe for the topical uses it is actually marketed for, which typically involve substantial dilution, but it does mean that undiluted or high-concentration dermal application, the kind sometimes recommended in informal aromatherapy guidance, sits outside the exposure conditions that most safety data were generated under.

Regulatory Safety Assessments

Regulatory evaluation of thyme oil has matured considerably in the past decade, helped along by the broader push within the EU to formally re-assess botanical feed and flavouring additives against modern toxicological data requirements. The EFSA Panel on Additives and Products or Substances used in Animal Feed evaluated an essential oil obtained from the flowering aerial parts

of *T. vulgaris* and/or *T. zygis* for use across all animal species, working through acute, repeated-dose, genotoxicity, and target-species tolerance data submitted by the applicant, and concluded that the additive was safe for the target species and consumers of animal products at the proposed use levels, while flagging the oil as an eye and skin irritant and a potential dermal sensitizer for those handling it during manufacture [22]. That combination of conclusions — safe as a dietary constituent at intended use levels, but requiring occupational handling precautions — captures the overall shape of the toxicological picture better than any single study could on its own.

Discussion and Knowledge Gaps

Put the pharmacology and the toxicology side by side and a fairly coherent, if incomplete, story emerges. The antimicrobial, antioxidant, and spasmolytic activities of thyme oil are reasonably well supported mechanistically and are broadly consistent with the traditional indications the plant has accumulated over centuries of use, which is more than can be said for a lot of botanicals under pharmacological scrutiny. The toxicological data, likewise, do not point to any acute hazard at doses relevant to normal use, and the genotoxicity work on thymol and carvacrol is reassuring rather than alarming.

That said, several gaps are worth naming plainly rather than glossing over. First, chemotype heterogeneity is rarely controlled for across the pharmacological literature — a study reporting "*Thymus vulgaris* essential oil" activity may be describing an oil with anywhere from near-zero to 45%+ thymol content, and pooling such studies into general claims about "thyme oil efficacy" risks averaging together preparations that behave quite differently in vivo. Second, almost none of the clinical evidence for respiratory benefit — including the largest and best-conducted studies — actually tests the distilled essential oil; it tests hydroalcoholic or aqueous extracts, and the assumption that oil-based products share the same efficacy is plausible but empirically untested. Third, repeated-dose toxicity data remain limited essentially to a single well-conducted 28-day rat study; longer-duration and reproductive/developmental toxicity data specific to the whole essential oil (as opposed to isolated thymol or carvacrol) are thin, which matters for any regulatory extension beyond the current approved use levels. Finally, the dermal sensitization risk, while well documented in case reports, has not been quantified in a way that lets formulators set confident maximum-use concentrations for leave-on cosmetic or topical products — most of the guidance in circulation is more cautious tradition than quantitative risk assessment.

Conclusion

Thymus vulgaris essential oil sits in a comparatively favourable position among widely used botanicals: its traditional uses map reasonably well onto demonstrated pharmacological activity, its acute and short-term toxicity profile is benign at doses consistent with normal use, and its genotoxic potential appears low based on the constituent-level data available. The oil is not risk-free — dermal sensitization is real and occupationally relevant, and the repeated-dose safety margin narrows once exposure moves well above dietary or standard medicinal levels — but nothing in the current literature suggests a hazard disproportionate to what regulators have already built into existing use restrictions. What the field genuinely needs now is less another antimicrobial screening study and more chemotype-standardized pharmacological work paired with longer-duration toxicological studies on the whole oil itself, so that safety conclusions currently resting on isolated thymol and carvacrol data can be extended with confidence to the complex mixtures that actually reach consumers.

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