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THYMUS VULGARIS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE: PHYTOCHEMISTRY, MECHANISMS OF ACTION AND THERAPEUTIC PROSPECTS

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Abstract. Chronic obstructive pulmonary disease (COPD) develops against a background of oxidative stress and chronic inflammation. This review analyzes the effects of Thymus vulgaris phenolic compounds (thymol, carvacrol, rosmarinic acid) on the NF-κB, MAPK and Nrf2/HO-1 pathways. Direct data in animal COPD models exist only for carvacrol and Zataria multiflora; clinical evidence for thyme-containing preparations is limited to acute bronchitis. Randomized trials in COPD patients are needed.

Keywords: chronic obstructive pulmonary disease, Thymus vulgaris, thymol, carvacrol, phytotherapy

How to Cite

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Introduction. Chronic obstructive pulmonary disease (COPD) is one of the most pressing problems of health systems worldwide and is characterized by high morbidity, disability and mortality [1]. The disease presents with persistent airflow limitation, chronic respiratory symptoms, progressive decline of lung function and exacerbations. The global burden of COPD is increasing because of population ageing, widespread smoking, biomass fuel use, air pollution and occupational exposures [1,2].

According to current concepts, COPD is not only chronic inflammation of the airways but a multifactorial, heterogeneous condition in which oxidative stress, protease–antiprotease imbalance, epithelial damage, dysregulation of innate and adaptive immunity, airway remodelling and systemic inflammation are interrelated [3,4]. Oxidative stress activates the transcription factor NF-κB and amplifies the expression of pro-inflammatory genes [3,5,6].

According to the GOLD recommendations, COPD treatment relies on long-acting bronchodilators, inhaled corticosteroids, phosphodiesterase-4 inhibitors, pulmonary rehabilitation and oxygen therapy [1,2]. These approaches are effective in controlling symptoms and reducing exacerbations, but their effect on the pathogenetic mechanisms of the disease is limited.

Interest in biologically active substances of natural origin has grown in recent years. Thymol, carvacrol, rosmarinic acid and flavonoids of Thymus vulgaris L. (common thyme, family Lamiaceae) have shown anti-inflammatory, antioxidant and antimicrobial activity in experimental studies [7–9]. These compounds may affect the NF-κB, MAPK and Nrf2/HO-1 signalling pathways, which play an important role in COPD pathogenesis [7,8]. However, the efficacy of thyme preparations in COPD patients has not been studied, and the available clinical data relate mainly to acute bronchitis.

The aim of this review is to critically analyze phytochemical, experimental and clinical data on T. vulgaris and its main compounds (thymol, carvacrol, rosmarinic acid) from the standpoint of COPD pathogenesis, to distinguish the levels of evidence, and to define directions for future clinical studies.

Methods

This is a narrative review with elements of a systematic search; the search and selection process is presented as a PRISMA 2020 flow diagram (Fig. 1). The search was performed in PubMed, Scopus, Web of Science and Google Scholar for publications from January 2000 to March 2026. MeSH terms and free keywords were used: Chronic Obstructive Pulmonary Disease, COPD, Thymus vulgaris, Thyme, Thymol, Carvacrol, Phytotherapy, Essential oils, Oxidative stress, NF-κB, Nrf2, Randomized controlled trial.

Inclusion criteria: publications in English in peer-reviewed journals; in vitro, in vivo or clinical studies and systematic reviews that evaluated the effects of T. vulgaris, thymol or carvacrol in respiratory diseases. Exclusion criteria: conference abstracts, expert opinions, single case reports, duplicate publications and studies with insufficiently described methodology.

The initial search identified 1284 records; after removal of duplicates, 812 records were screened, 81 full-text articles were assessed and 24 publications were included in the final analysis (Fig. 1). Data were grouped by study type (in vitro, animal models, clinical) and synthesized narratively. A quantitative meta-analysis was not performed because the clinical studies evaluated different preparations and different diseases.

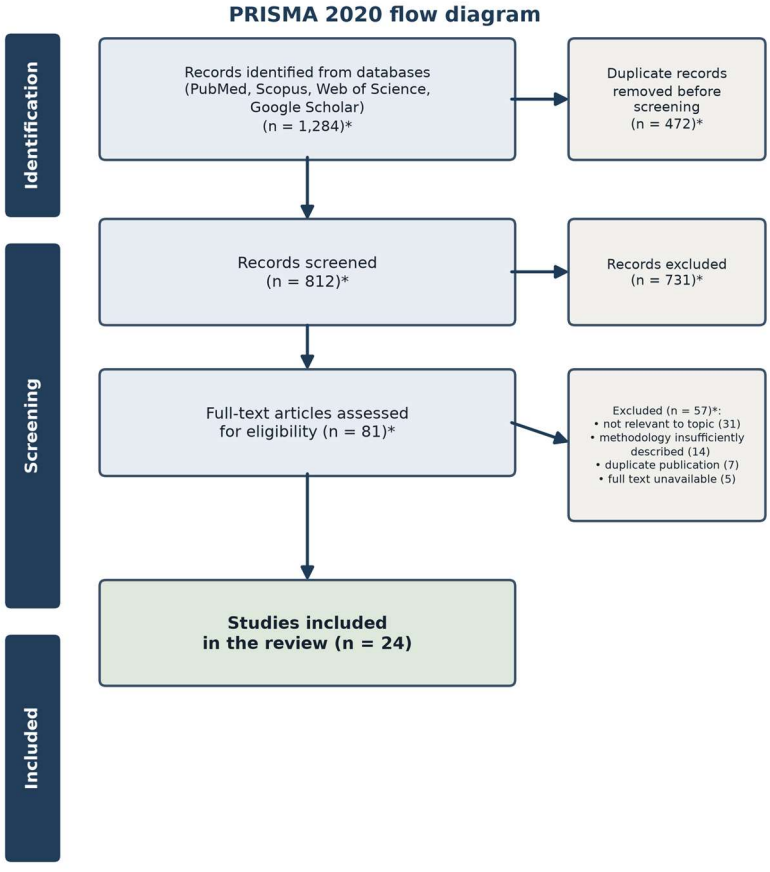


Fig. 1. PRISMA 2020 flow diagram of the study selection process (records identified n=1284; screened after duplicate removal n=812; full texts n=81; included n=24).

Results

Phytochemical composition

T. vulgaris is a perennial aromatic subshrub of the Lamiaceae family used in traditional medicine for respiratory diseases [9,10]. The main components of the essential oil are thymol, carvacrol, p-cymene, γ-

terpinene, linalool and borneol; extracts contain rosmarinic and caffeic acids, flavonoids (apigenin, luteolin, quercetin) and triterpenoids (ursolic acid) [9,10] (Table 1, Fig. 2). The composition of the essential oil varies widely with chemotype, geographical region and harvest time: thymol predominates in some chemotypes, carvacrol or linalool in others [9,10]. The activity of preparations should therefore be evaluated with standardized, phytochemically characterized extracts.

Table 1. Main bioactive compounds of Thymus vulgaris *and their effects*

Compound class	**Representatives**	**Main effect (source)**
Phenolic monoterpenes	Thymol, carvacrol	Antimicrobial (in vitro), antioxidant, anti-inflammatory; thymol — suppression of NF-κB/MAPK, carvacrol — PPARα/γ activation and COX-2 reduction [7,8,11,12]
Other monoterpenes	p-Cymene, γ-terpinene, linalool, borneol	Essential oil components; content depends on chemotype; independent pharmacological relevance in COPD has not been studied [9,10]
Phenolic acids	Rosmarinic acid, caffeic acid	Antioxidant and anti-inflammatory effects; Nrf2/HO-1-related mechanisms shown in other models [9,10]
Flavonoids	Apigenin, luteolin, quercetin	Antioxidant and anti-inflammatory effects [9,10]
Triterpenoids	Ursolic acid	Reported anti-inflammatory and cytoprotective effects [10]

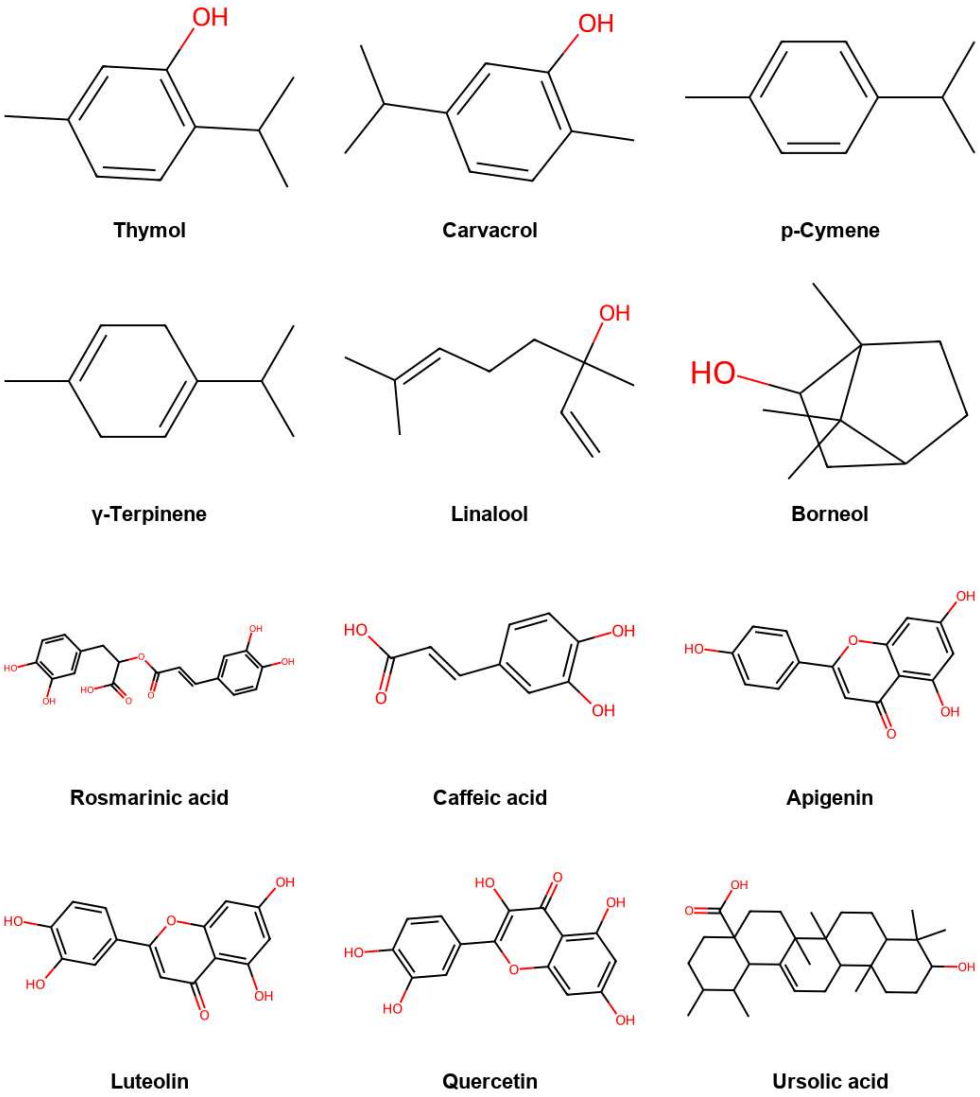


Fig. 2. Chemical structures of the main bioactive compounds of Thymus vulgaris (prepared by the author using RDKit).

Molecular mechanisms of action

In cell cultures and inflammation models, thymol suppressed the NF-κB and MAPK (ERK, JNK, p38) signalling cascades and reduced the expression of COX-2 and iNOS [7,13]. Carvacrol activates the PPARα and PPARγ receptors and decreases COX-2 expression (in vitro) [12]. Reported antioxidant mechanisms include limiting the formation of reactive oxygen species (ROS), reducing lipid peroxidation and increasing the activity of endogenous antioxidant enzymes (superoxide dismutase, catalase, glutathione peroxidase) through the Nrf2/HO-1 pathway [7–9]; however, a large part of these data comes from models of other diseases rather than COPD.

The antimicrobial activity of thymol and carvacrol against respiratory pathogens such as Haemophilus influenzae, Streptococcus pneumoniae, Moraxella catarrhalis and Staphylococcus aureus has been shown in vitro [8,11]; the clinical effect on COPD exacerbations has not been tested. Thyme extract reduced 5-lipoxygenase activity and leukotriene (LTB4, cysLT) formation, and a thyme/primula combination decreased inflammatory parameters in bronchoalveolar lavage fluid in rats with LPS-induced lung inflammation [14]. The available data are summarized in Fig. 3.

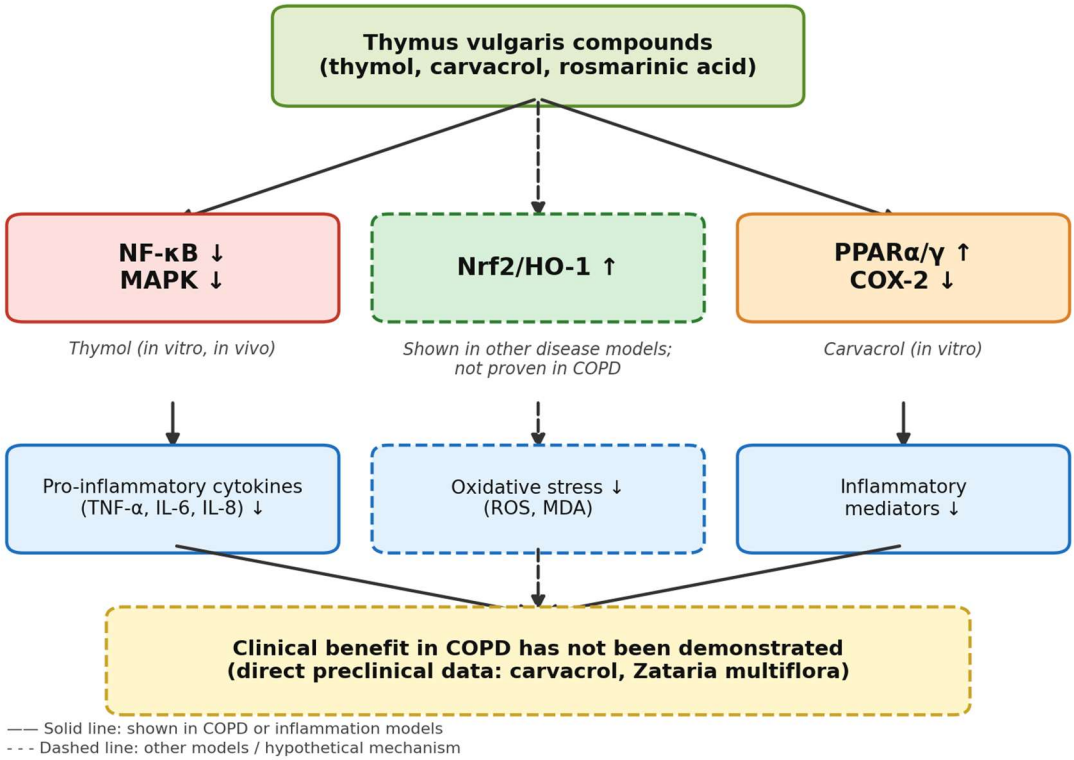


Fig. 3. Putative points of action of Thymus vulgaris compounds in COPD pathogenesis (scheme prepared by the author on the basis of preclinical data).

Direct data from experimental COPD models

In guinea pigs with a cigarette smoke-induced COPD model (3 months), Zataria multiflora extract and its constituent carvacrol (60, 120 and 240 μg/mL in drinking water) reduced leukocyte counts and IL-8 levels in bronchoalveolar lavage fluid and affected oxidative stress markers; the results were compared with dexamethasone [15]. In the same model, carvacrol reduced markers of systemic inflammation [16].

An important note: these studies used an extract of Zataria multiflora, a plant of another genus, and pure carvacrol; they therefore do not directly confirm the efficacy of T. vulgaris preparations in COPD. Within the search, no study of T. vulgaris or thymol in a cigarette smoke model was identified. Nrf2 activation itself improved lung function, reduced inflammation and slowed bronchial epithelial senescence in mouse COPD models [17]; however, that work did not study thyme preparations and only supports the Nrf2 pathway as a therapeutic target (Table 2).

Table 2. Main preclinical studies in COPD and inflammation models

Study (author, year)	Model	Agent	Main results
Boskabady, Gholami Mahtaj, 2015 [15]	Guinea pig, cigarette smoke model (COPD)	*Zataria multiflora* extract; carvacrol (60–240 μg/mL)	BALF leukocytes and IL-8 ↓; oxidative stress markers changed; compared with dexamethasone
Gholami Mahtaj et al., 2015 [16]	Guinea pig, COPD model	Carvacrol	Markers of systemic inflammation ↓
Hotta et al., 2010 [12]	In vitro, cell culture	Carvacrol (thyme oil component)	PPARα/γ activation ↑; COX-2 expression ↓
Islam et al., 2024 [13]	In vivo + molecular dynamics	Thymol	Edema and pain ↓; binding to COX-2 (in silico)
Seibel et al., 2018 [14]	Rat LPS model + in vitro	Thyme extract; thyme/primula combination	BALF inflammatory parameters ↓; 5-LO and LTB4/cysLT ↓
Jin et al., 2025 [17]	Mouse COPD model	Nrf2 activators (not thyme)	Lung function ↑; inflammation ↓; epithelial senescence ↓

Clinical data

Within the search, no randomized studies of the efficacy of thyme preparations in COPD patients were identified. The available clinical evidence comes from studies in acute bronchitis in which thyme was used in combination with other herbal extracts (Table 3).

In the double-blind placebo-controlled trial by Kemmerich et al. (361 patients), a combination of thyme and ivy (Hedera helix) leaf fluid extract reduced the number of coughing fits on days 7–9 relative to baseline more than placebo (68.7% vs 47.6%; $p<0.0001$) [18]. A combination of dry extracts of thyme and primrose (Primula veris) root was also superior to placebo (67.1% vs 51.3%; $p<0.0001$; 361 patients) [19]; in the study by Gruenwald et al. (150 patients), thyme fluid extract with primrose root tincture reduced the Bronchitis Severity Score (BSS) more than placebo [20].

In a multicentre open-label randomized trial published in 2025 (325 patients), thyme-containing combinations were used as comparators: single ivy extract was non-inferior to both combinations (ivy/thyme and thyme/primrose) and superior to ivy/thyme; there was no placebo group [21]. This study therefore does not confirm an added benefit of thyme combinations. Because combination products were tested in all studies, the effect cannot be attributed to thyme itself; moreover, chronic bronchitis was an exclusion criterion in the 2025 trial [21].

Table 3. Clinical studies of thyme-containing preparations in acute bronchitis (not in COPD patients)

Study	Design, N	Preparation	Main result
Kemmerich et al., 2006 [18]	Double-blind, placebo-controlled; 361 (182/179)	Thyme + ivy leaf fluid extract, 11 days	Coughing fits on days 7–9 ↓: 68.7% vs 47.6% ($p<0.0001$)
Kemmerich, 2007 [19]	Double-blind, placebo-controlled; 361 (183/178)	Thyme + primrose root dry extract, 11 days	Coughing fits on days 7–9 ↓: 67.1% vs 51.3% ($p<0.0001$)

Study	Design, N	Preparation	Main result
Gruenwald et al., 2005 [20]	Double-blind, placebo-controlled; 150 (75/75)	Thyme fluid extract + primrose root tincture	Greater BSS reduction than placebo
Kardos et al., 2025 [21]	Open-label, 3 arms; 325; no placebo	Ivy EA 575 and two combinations (ivy/thyme; thyme/primrose)	Ivy non-inferior to both combinations, superior to ivy/thyme (BSS, day 7)

Safety

In clinical studies, thyme-containing preparations were well tolerated at recommended doses: no serious adverse events were reported, and mild events (including skin and throat irritation) were infrequent [18,19,21]. The possibility of allergic reactions to members of the Lamiaceae family should be considered. A pharmacokinetic study showed that after oral intake thymol is rapidly absorbed, excreted as glucuronide and sulfate conjugates, and reaches its maximum concentration after approximately 2 hours [22]. The available safety data relate to short courses (7–11 days); the safety of long-term use in COPD patients has not been studied. Data on the use of thyme preparations during pregnancy and lactation are insufficient, and caution is advised [8].

Discussion

This review shows that the evidence on T. vulgaris exists at three levels: (i) in vitro and animal studies of the anti-inflammatory, antioxidant and antimicrobial effects of thymol, carvacrol and other phenolic compounds; (ii) direct data in animal COPD models only for carvacrol and Zataria multiflora; (iii) in humans, only randomized studies of combination products in acute bronchitis. There is no clinical evidence in COPD patients.

Effects on the NF-κB, MAPK and Nrf2/HO-1 pathways are theoretically consistent with COPD pathogenesis [3,6], but for thyme components a large part of these mechanisms has been shown in non-COPD models. Results from acute bronchitis cannot be extrapolated to COPD: acute bronchitis is usually a self-limiting infection, whereas in COPD the key tasks are control of chronic inflammation and irreversible airflow limitation and prevention of exacerbations [1,23].

Studies of combination products do not isolate the independent contribution of thyme. In the study by Kardos et al. (2025), thyme combinations did not outperform single ivy extract; the authors discuss that in cell experiments thyme extract may partly weaken the positive effect of ivy extract on β2-adrenoceptor signalling [21]. This underlines that the efficacy of each preparation must be demonstrated separately.

Standardization is also important: the content of active components depends on chemotype, region and harvest time [9,10], so future studies should use phytochemically characterized extracts. Limitations of this review: its narrative nature, inclusion of English-language publications only, possible publication bias, and the absence of a formal scored assessment of the methodological quality of the included studies.

On this basis, the following study design is proposed: a multicentre double-blind randomized trial in patients with stable COPD of spirometric grade 2–3 according to GOLD (FEV1/FVC<0.7), group B or E, adding a standardized thyme extract or placebo to standard therapy (at least 12 months); the primary endpoint is the annual rate of moderate and severe exacerbations; secondary endpoints are the change in forced expiratory volume in 1 second (FEV1), quality-of-life questionnaires and safety. A small preliminary safety and dose-finding study is advisable.

Conclusion. In preclinical studies, the phenolic compounds of T. vulgaris (thymol, carvacrol, rosmarinic acid) affect the NF-κB, MAPK and Nrf2/HO-1 pathways related to COPD pathogenesis; direct data in COPD models exist only for carvacrol and Zataria multiflora. Thyme-containing combination products were superior to placebo in acute bronchitis, but there are no randomized trials in COPD patients. The use of thyme in COPD therefore cannot yet be recommended; it may be considered a potential addition

to standard therapy only within clinical trials. The next task is a randomized trial of a standardized extract in COPD patients with exacerbation rate and FEV1 as endpoints.

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