

Thyme

Thymus vulgaris

AN OVERVIEW OF ITS BIOLOGICAL ACTIVITIES AND MECHANISM OF ACTIONS

Scientific report
authored by



Thyme (*Thymus vulgaris*), is an **aromatic plant**, from the Lamiaceae family, widespread around the **Mediterranean region** and also worldwide distributed. Thyme is characterized by a large number of chemotypes and can be used in its crude herb form, particularly in warm infusions (teas), as an extract or for its richness in essential oil. Thyme is traditionally used to relieve **symptoms cough and as an expectorant for productive (chesty) coughs associated with colds.**

Physiology and management of respiratory infections

Acute respiratory tract infections are among **the most prevalent diseases in general and pediatric practice**, particularly during the winter months, accounting for up to 50% of medical consultations during epidemics. During this period, the respiratory tract is frequently exposed to pathogens that can lead to respiratory infections. Upper respiratory tract infections (URTI) include the common cold, epiglottitis, laryngitis, pharyngitis (sore throat), and sinusitis (sinus infection), while lower respiratory tract infections include bronchitis, bronchiolitis, chest infections, and pneumonia. Influenza can affect both the upper and lower respiratory tracts. These diseases are primarily caused by viruses (90-95%), such as adenoviruses, coronaviruses, influenza viruses (A, B), parainfluenza viruses, respiratory syncytial virus, and rhinoviruses, although secondary bacterial infections can sometimes occur.

The foundation of every infection lies in a disturbed immune balance. The immune system can be weakened by **external factors** (dry heated air and cold, damp weather) and **immune-modulating processes** (stress response). Pathogens often evade the immune defense system through rapid replication. **Infections develop in three stages** through interactions with epithelial cells. Pathogens that penetrate deeper cell layers can serve as reservoirs for prolonged infections and recurrences of respiratory tract infections [1, 2].

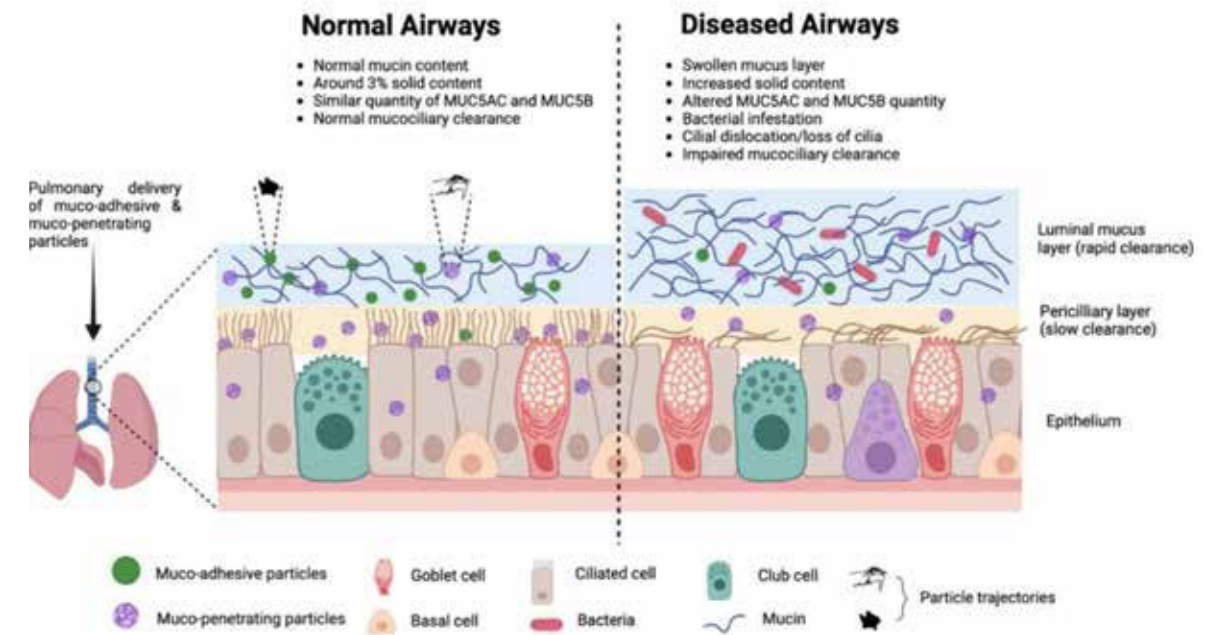


Figure 1 : Modification of mucus production on normal and diseased airways (Pangeni et al., 2023).

These pathogens trigger a **cascade of immunological and epithelial cell reactions**, leading to increased inflammation. This physiological response to pathogens, allergens, and injuries is characterized by the production of **pro-inflammatory cytokines** from various cell populations, resulting in the development of upper respiratory tract symptoms (rhinorrhea, sore throat, etc.) [2]. One of the most common symptoms for URTI is the **excess production of mucus** associated with rhinorrhea or productive cough during bronchitis for example.

If mucus production is crucial in a healthy state, the **production is altered during an infection**. Hence, healthy individuals produce mucus continuously to protect the airways and humidify the air. In respiratory diseases, the composition and properties of airway secretions change, leading to **mucus hypersecretion that disrupts mucociliary clearance and airflow**, causing mucus retention. Mucus from individuals with respiratory diseases often has **increased viscoelasticity, leading to buildup in the airways and deterioration of lung function and nose congestion** [2,3].

The medical approach to cope with URTI is a **symptomatic approach** except when a bacterial infection is confirmed, antibiotics can be used. A **complementary approach can be interesting**, when possible, with plants traditionally used in respiratory tract infections, such as thyme.

Thyme (*Thymus vulgaris*)

Thyme is a grassy annual plant belonging to the Malvaceae family. It belongs to the *Thymus* genus, which comprises over **3000 species, including thyme and wild thyme**. Thyme is characterized by a large number of chemotypes (α -terpineol, thymol, carvacrol, geraniol, linalool, p-cymene and thujanol) which modifies its biological properties. The fresh or dried herb of thyme and the essential oil produced by the **steam distillation of the fresh flowering tops are both employed for their properties**. The main active constituents, depending on chemotype and extracts include notably terpenes, phenols, thymol, carvacrol, glycosides of phenolic monoterpenoids, and rosmarinic acids [4].

Biological properties of thyme

As reported in several monographies, thyme has been used traditionally for its benefits for the respiratory tract (such as a balanced inflammatory response, and a healthy productive cough) [4-6].

The scientific literature confirmed those traditional uses and effects. In preclinical studies, aerial part extracts of thyme demonstrated a **potent relaxant effect on tracheal smooth muscles and tracheal chains comparable to that of theophylline**, indicating its **bronchodilatory potency** in the respiratory tract [7].

The beneficial effect of thyme on the respiratory tree has also been proven in humans with double-blind studies in children and adults, especially combined with ivy and primula extracts [8, 9]. These mixes contain thyme extract as the major ingredient representing 90% and 60% of the final preparations, respectively. In a placebo-controlled, double-blind multicenter study, the efficiency of fixed combination of dry extracts of thyme herb and primula root in adults suffering from acute bronchitis with productive cough was evaluated. Reduction of coughing fits compared to baseline was higher in the treated group compared to the control group (67.1% in verum vs. 51.3% in placebo group)(Figure 2). Additionally, the responder rate for bronchitis severity score improved more rapidly, in responders in the treated group than in the placebo group (visit 2: verum 77.5%, placebo 60.1%; visit 3: verum 92.9%, placebo 75.8%) (Figure 3) [8].

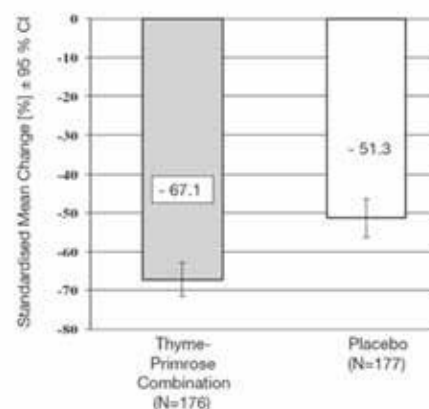


Figure 2: Standardized change [%] in coughing fits on Day 7-9 +/6 CI (FAS: N = 353; 7 patients not evaluable due to missing values at baseline) (Kemmerich et al., 2007)

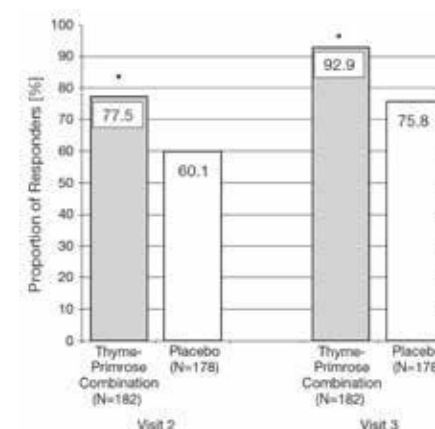


Figure 3: Proportion of responders [%] at Visit 2 and visit 3 (FAS). Significant difference on a-level = 0,05 (*) between thyme-primrose combination and placebo at Visit 2 (Chi-square test, p = 0,0006) and Visit 3 (Chi-square test, *p < 0,0001). (Kemmerich et al., 2007).

Finally, the combination of thyme and primula facilitate mucus lysis and expectoration, improving the quality of life of the subjects included in the study [8]. The effect of the efficacy of the association between thymus and ivy extract on bronchitis was also confirmed in a double-blind, placebo controlled, multicenter study including subjects suffering also from bronchitis. A significant and clinical improvement of bronchitis severity score, coughing fits, sleep disturbance induced by coughing and improvement in the ability to cough up mucus during daytime and patient's general well-being was reported [9]. In both studies the safety and the tolerability of the test products were confirmed [8, 9].

In children with acute asthma, a thyme-based syrup administered every eight hours significantly reduced coughing and improved respiratory function compared to the control group, suggesting its potential use as an adjunct in asthma exacerbation management [10].

As infection of the respiratory tract involves multifactorial mechanisms, it is not unusual to see that some plant combinations could be of interest to relieve the symptomatology of bronchial function alteration. Nevertheless, the effect of thymus extract seems to be the most important as it represents the majority part of the compounds in the end-products tested and its efficacy as a mono-ingredient in respiratory issues was confirmed in children.

Mechanism of actions

The effect on **inflammatory cytokines of SYMTHYM™** was evaluated internally in reconstructed human oral epithelium by the quantification of interleukin-6 (IL-6) production in response to a pro-inflammatory agent, lipopolysaccharide (LPS) from *Pseudomonas aeruginosa* (unpublished data). The reconstructed human oral epithelium consists of a multilayer three-dimensional culture of keratinocytes exhibiting *in vivo*-like composition and morphological characteristics. The highest dose of SYMTHYM™ tested, decreased IL-6 production by 59% (p<0.05) when the cells were pretreated with LPS compared to control (LPS + vehicle).

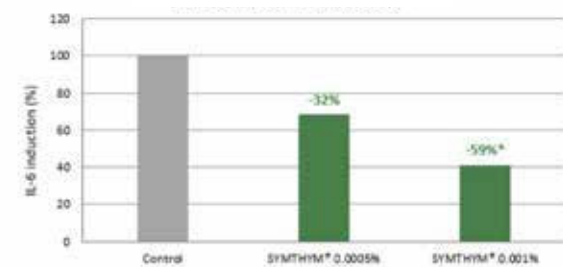


Figure 4: Effect of SYMTHYM™ on IL-6 production after a LPS challenge in an *in vitro* reconstructed human oral epithelium.

* p < 0.05; Mann-Whitney test VS 'Control'

Another feature of aerial tree **infection is the presence of oxidative stress**. DPPH test is widely used to evaluate the antioxidant capacity of molecules or plant extracts. In this test, SYMTHYM™ has a significant dose-dependent antioxidant activity that surpasses the one of a standard molecule used as a positive control (Trolox).

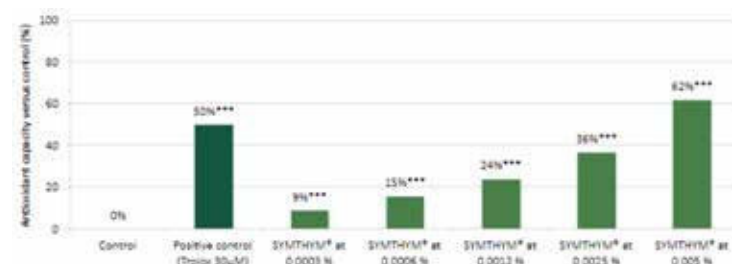


Figure 5: Antioxidant effect of SYMTHYM™ (DPPH - internal data)

*** p < 0.001; Student's t test VS 'Control'

These results confirm that the extract possesses *in vitro* antioxidant activity and supports the healthy inflammatory response. The *in vitro* positive effects of this thyme extract on oxidative stress and inflammation could be attributed to its richness of polyphenols notably in rosmarinic acids as already demonstrated for others type of extracts in the literature (for review see [11, 12]).

As previously said, the medical approach is mainly symptomatic, except when a bacterial infection is confirmed or when an anti-viral approach is necessary. **Thyme possesses the ability to tackle pathways involved in the pathogenesis of infection** of the respiratory tree but to act also on the root cause of the infection thanks to its antimicrobial effects. Indeed, several preclinical studies demonstrated that

thyme extracts and its essential oil exhibit **antimicrobial effects** both on viruses and bacterial strains [11].

Another mechanism that could be modified during bronchial infection is mucociliary clearance. Mucociliary clearance is a first line of defense, when we inhaled particles such as dust and bacteria. This mechanism **prevents the accumulation of particles and mucus** within the lungs [13]. This system of defense can temporary dysfunction caused by infection for example, or environmental agents like in longstanding cigarette smokers (COPD - Chronic obstructive pulmonary disease). In this context, the modulating effect on cilia beating frequency of an ethanolic thyme extract was tested in a MucilAir 3D human COPD airway epithelium reconstituted *in vitro* system. The commercial thyme extract tested increased the cilia beating frequency in airway epithelia from COPD donors [14].

Some data indicated that **antispasmodic activity** on rat trachea and ileum and increase the mucociliary transport in mice through a modulatory action on the β 2-receptor system adrenergic and histamine H1 receptor.

Conclusion

Thyme's uses for the upper respiratory tract have a **long traditional history in many parts of the world**. Preclinical and clinical data confirmed those effects and emphasis some mechanisms of actions involving **antioxidant activities** and **improving and alter inflammatory response through a complex alteration of mucociliary clearance**. Its traditional use is recognized in several monography.



Why Groupe Berkem?

✓ Pioneer in plant extraction for over 60 years

✓ In-house manufacturer

✓ R&D innovation

✓ Ethical and premium sourcing



✓ Tailor-made ingredient development

✓ Premium nutraceutical range

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