Medicinal properties of *Thymus vulgaris* essential oil: a review

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Abstract

Globally, the interest in essential oils has been steadily increasing over the last decades due to their beneficial health effects and the wide range of applications that are directly linked to a variety of pharmacological and biological activities. Thymus vulgaris L., also called common or garden thyme is a small perennial herb, which has been used over the years as food additive, but also as a valuable cure in several pathologies. It is believed that the medicinal properties of Thymus vulgaris are attributed to its essential oil, which is a mixture of monoterpenes. Moreover, the therapeutic properties of this essential oil are due to its main compounds, namely the terpenoid thymol and its phenol isomer carvacrol. Several investigations have indicated that thyme oil possesses strong antiseptic, antimicrobial, antifungal, antioxidant effects and therefore, all the aforementioned features make this essential oil a promising remedy in human and veterinary medicine fields. The aim of the present study was to review and highlight the medicinal attributes of Thymus vulgaris essential oil, apart from its nutritional value, in order to identify novel alternative cures in the treatment of both humans and animals diseases.

Keywords: *essential oil, medicinal properties, Thymus vulgaris.*

Introduction

Thymus vulgaris L., one of the most famous aromatic plants in the *Lamiaceae* family and belonging to the genus *Thymus,* is highly recommended by researchers due to numerous therapeutic promises of its essential oil, commonly known as thyme oil (Zaidi and Crow, 2005; Maksimoviæ et al., 2008; Sokoviæ et al., 2009).

In general, essential oils may contain around 20-80 phytochemicals (Regnault-Roger et al., 2012). Concerning *Thymus vulgaris,* there are several chemotypes which are named in accordance with the major compound, for instance, thymol, carvacrol, terpineol and linalool. In addition to this, Sienkiewicz et al. (2017) reported that thyme oil consists mainly of thymol (38.1%), p-cymene (29.1%), γ-terpinene (5.2%), linalool (3.7%) and carvacrol (2.3%). Moreover, it has been stated that the biological properties of thyme oil are primarily due to its main constituents, thymol and carvacrol (Newton, 2000).

Besides the fact that thyme oil is one of the most popular essential oils in the food and cosmetics industries, many studies underlined its therapeutic potential in various pathologies (Stahl-Biskup, 2002; Burt, 2004; Shin and Kim, 2005; Politeo et al., 2007).

The present study was designed to highlight and summarize some of the medicinal properties of *Thymus vulgaris* essential oil, which lately, has gained more and more attention from researchers around the world.

Antimicrobial, antioxidant, anticancer effects

Also known as volatile oils, essential oils are natural aromatic compounds, nontoxic and nonpollutive products, presenting low risk of adverse effects and low risk of microbial resistance development (Rajkowska et al., 2014). The antimicrobial capacity of essential oils depend, in general, on their chemical compounds, mostly on their phenolic compounds, such as thymol, γ-terpinene, carvacrol (Boruga et al., 2014; Cristiani et al., 2007). Thymol has registered 30 times stronger antibacterial activity and 4 times lower toxicity compared to phenol, an antiseptic that can be found in several herbicides (Hajimehdipoor, 2010; Weber, 2004). Furthermore, thymol appears to disrupt the membrane structure and to increase the cell permeability, leading to a proton motive force diminution and decreased ATP intracellular levels, and hence, causing the death of the pathogen cell (Liolios et al., 2009; Fong et al., 2011). Another constituent present in essential oils composition is p-cymene, which seems to exhibit an antibacterial activity only when it is used with thymol and γ-terpinene, proving synergistic effects (Rota et al., 2008).

Several studies demonstrated the efficacy of thyme essential oil against numerous pathogens (Lai and Roy, 2004; Mitsch et al., 2004; Penalver et al., 2005; Al-Bayati, 2008). In this regard, a strong antimicrobial activity was recorded against *Helicobacter pylori, Salmonella typhimurium, Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumoniae, Enterococcus faecalis, Staphylococcus aureus, Staphylococcus epidermidis, Selenomonas artemidis, Porphyromonas gingivalis, Streptococcus mutans, Streptococcus sobrinus, Streptococcus spp., Pantoea spp., Bacillus spp., Shigella spp* (Ceyhan and Ugur, 2001; Boruga et al., 2014; Imelouane et al., 2009; Nasir et al., 2015). Additionally, it was evaluated the growth inhibition effects of thyme esential oil against various strains of both Gram-negative and Gram-positive bacteria (Marino and Bersani, 1999; Prasanth et al., 2014; Saleh et al., 2015). A strong antimicrobial activity was observed against both types of bacteria, but however, it was more pronounced against the Gram-positive bacteria.

Likewise, other researchers pointed out that thyme oil is highly effective against different types of fungi and yeast, such as *Aspergillus flavus, Aspergillus parasiticus, Aspergillus niger, Trichophyton spp., Microsporum spp., Rhodotorula rubra and Candida albicans* (Arras and Usai, 2001; Inouye et al., 2001a; Nasir et al., 2015; Rajkowska et al., 2014). Moreover, Jabeur et al. (2017) reported that thyme essential oil is active against the plant-pathogenic fungus *Mycosphaerella graminicola*, responsible for septoria tritici blotch (STB), one of the most economically important diseases of wheat, which threatens global food production. Furthermore, Nolkemper et al. (2006) revealed a strong antiviral activity of thyme essential oils against Herpes simplex virus type 1 (HSV-1) and acyclovir-resistant strain of HSV-1.

Antioxidants are compounds which are able to inhibit different oxidation reactions and to remove free radical intermediates and thus, preventing cell death (Dipak, 2013). The antioxidant capacity of thyme essential oil is due to the presence of its active compounds, mainly thymol and carvacrol (Ruberto and Baratta, 2000). In *vivo* and *in vitro* studies showed important antioxidant effects of thyme oil and thymol (Youdim and Deans, 2000; Nickavar et al., 2005).

Thyme oil also contains significant amounts of zeaxanthin, apigenin, lutein, luteolin and thymine, which represent a valuable source of antioxidants (Dauqan and Abdullah, 2017). The flavonoids may prevent the release of superoxide anion and protect erythrocytes from oxidative stress (Youdim and Deans, 2000). Moreover, El-Nekeety et al. (2011) evaluated the protective effects of thyme oil against aflatoxin-induced oxidative stress in male Sprague-Dawley rats. The animals were divided into six groups and treated for 2 weeks: control group; the groups treated orally with low and high doses of thyme oil; the group fed AFs (aflatoxins)-contaminated diet and the groups fed AFs-contaminated diet and treated orally with the oil at the two tested doses. The results highlighted a disturbance in serum lipid profile, a low antioxidant capacity, increased creatinine, uric acid and nitric oxide in blood serum, lipid peroxidation in liver and histological changes within the liver tissues, when applying the treatment with aflatoxins; the oil at different doses did not seem to produce any significant changes. An improvement was however observed in the investigated parameters and histological aspects, when using the combined treatment.

Available data have suggested that foods which are rich in phytochemicals, can reduce the risk of various types of cancer, due to their antioxidant, anti-inflammatory and immunomodulatory activity and have the ability to modulate the proliferation, apoptosis, angiogenesis of cancer cells (Kapinova et al., 2017; Kapinova et al., 2018; Stewart and Wild, 2014). According to Sertel et al. (2011), *Tymus vulgaris* essential oil inhibited the growth of human oral cavity squamous cell carcinoma, with the regulation of N-glycan biosynthesis and extracellular signal-regulated kinase 5 (ERK5) and interferon signaling. Furthermore, an *in vitro* study pointed out the antiproliferative and proapoptotic activity of thyme essential oil in MCF-7 cells and MDA-MB-231 cells, which are both breast cancer cell lines (Kubatka et al., 2019). Moreover, Kang et al. (2016) reported that thymol manifests anticancer activity by suppressing cell growth, inducing apoptosis, producing intracellular reactive oxygen species, depolarizing mitochondrial membrane potential, activating the proapoptotic mitochondrial proteins Bax, cysteine aspartases and poly ADP ribose polymerase in human gastric AGS cells, a human gastric adenocarcinoma cell-line.

Gastrointestinal health benefits

Numeorus research have been carried out in order to explore the gastrointestinal health benefits of thyme essential oil and particularly two of its most important constituents, thymol and carvacrol. In this regard, indigestion which is also known as dyspepsia could be treated by oral administration of thyme extract (Mossa et al., 1987). Moreover, it was reported that thymol and carvacrol may enhance the activities of intestinal and pancreatic trypsin, protease and lipase, when administered to animals in equal amounts. These two compounds also appear to ameliorate the liver function and increase appetite (Hosseinzadeh et al., 2015; Thompson et al., 2003; Hashemipour et al., 2013). Another research conducted by Höferl et al. (2009) suggested that thymol and carvacrol act as antispasmodic agents.

Thyme essential oil proved to be highly effective in several intestinal infections and infestations, namely hookworms, ascarids, Gram-positive and Gram-negative bacteria, fungi and yeasts, due to its valuable compounds (Ceyhan and Ugur, 2001).

Oliveira et al. (2012) revealed the carvacrol gastroprotective effects on experimentally induced gastric lesions in rats, by preventing the gastric epithelium injury. Furthermore, Silva et al. (2012) demonstrated that the oral administration of carvacrol reduced the gravity of chemically induced gastric damages in rats after two weeks of treatment by comparison to controls. Other researchers investigated the effect of thymol on differential gene expression in young pig gastric mucosa and they observed that this compound stimulates genes associated with mitosis, cell division regulation and the stomach digestive function (Colombo et al., 2014).

Thyme oil and oral care

Some of the most common and widespread oral pathologies are represented by dental caries, periodontal diseases and streptococcal pharyngitis. Dental caries, also known as tooth decay is the result of a complex interaction between acid producing tooth-adherent bacteria and fermentable carbohydrates leading to demineralization of the tooth and the formation of cavities. Dental caries aetiology involves microbial factors, fermentable carbohydrates, susceptible tooth surface (Petersen, 2005; Selwitz et al., 2007). The main microbial pathogen resposible for dental caries is *Streptococcus mutans*, a Gram-positive facultative anaerobe (Bowen and Koo, 2011; Gross et al., 2012). Different studies revealed the strong inhibitory effect of thyme essential oil on *Streptococcus mutans* growth (Ghorab et al., 2014; Hammad et al., 2007; Fani and Kohanteb, 2017; Gonçalves et al., 2011).

Periodontitis, or gum disease, represents a chronic inflammatory pathology which is activated by microbial agents and triggers the destruction of the tooth-supporting apparatus, causing tooth loss. The agents most frequently involved in the aetiology of periodontitis are considered to be *Aggregatibacter actinomycetemcomitans* and *Porphyromonas gingivalis* (Kononen et al., 2007). In this regard, there are some available data in literature regarding the inhibitory activity of thyme oil on the aforementioned pathogens (Rodriguez-Garcia et al., 2010; Fani and Kohanteb, 2017).

Streptococcuspyogenes (group A *Streptococcus*) is the most common and important cause of pharyngitis, a bacterial infection of oropharynx which involves tonsils and larynx. Since increasing failure to *Streptococcus pyogenes* treatment with penicillin and erythromycin has been noticed, because of allergy and antibioresistance, respectively, it is imperative to develop alternative natural antibacterial agents (Malli et al., 2010; Ying-Huang et al., 2014). Therefore, several research have emphasized gratifying results regarding *S. pyogenes* being highly sensitive to *Thymus vulgaris* oil (Inouye et al., 2001b; Solano et al., 2006; Sfeir et al., 2013; Nikolic et al., 2014; Fani and Kohanteb, 2017).

Thyme oil and wound healing

Due to its multiple biological properties, thyme oil can be regarded as a strong candidate concerning the development of products related to tissue repair. For instance, thymol and carvacrol, two major compounds detected in thyme oil seem to act in the wound healing phases. Thus, they have exhibited modulatory effect on the inflammatory cytokines and oxidative stress, during inflammatory phase and have enhanced re-epithelialization, angiogenesis and granulation tissue development, during proliferative stage. In the remodelling/maturation phase, they have increased the collagen deposition and have promoted the fibroblasts and keratinocytes growth (Komarcevic, 2000; Costa et al., 2019).

Additionally, thymol and carvacrol are able to activate antioxidant systems, as superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX), modulate reactive species and reduce inducible nitric oxide synthase (iNOS), one of the reactive oxygen (Andre-Levigne et al., 2017; Guvenc et al., 2018; Xiao et al., 2018). Another study conducted by Mollarafie et al. (2015) pointed out that a chitosan film consisting of pure thymol enhanced fibroblast cell growth. Likewise, Pivetta et al. (2018) reported that a gel containing nanoencapsulated tymol did not present any cytotoxicity in human keratinocytes, maintaining cell viability above 80%.

Conclusions

As we live in an era where pathogens have become more and more resistant to our arsenal of medications, there is an urgent need to explore and develop novel natural remedies in order to control public health threats. Thyme essential oil presents a high potential for the development of new therapeutic formulas in different kind of pathologies, due to its multiple biological activities. However, further research must be carried out in order to observe the efficacy and safety of these compounds, to discover the mechanisms of action, some of them being not yet fully understood or to make adjustments regarding dosage and treatment protocol.

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