Applications of thyme extracts on diseases of the oral cavity

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Abstract

For hundreds of years, herbal medicines have been used to treat various diseases of the oral cavity or to maintain oral hygiene. Currently, the growing resistance of microorganisms to the antimicrobials used, in combination with the emergence of emerging diseases, requires the urgent development of new, more effective drugs. Plants are a unique and renewable source for the discovery of new antimicrobial, antiinflammatory, antifungal, anticancer, etc. compounds.

The purpose of this article is to present the use of thyme extracts in diseases of the oral cavity, such as caries, gingivitis, periodontitis, oral cancer, oral candidiasis.

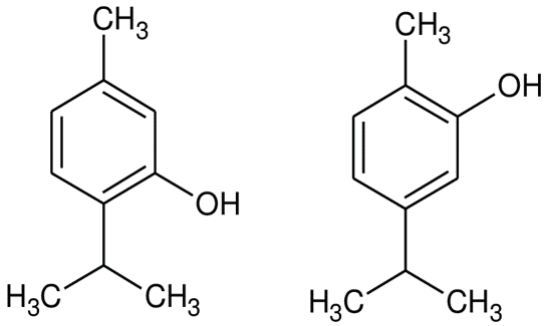
Keywords: Thyme, antimicrobial, anticancer, antifungal

INTRODUCTION

Thyme (Thymus vulgaris L.) is a plant native to the Mediterranean regions (Figure 1) commonly used as a culinary plant and also with a long history of use for various medicinal purposes [1]. Thyme, in the form of an infusion, was used as a mouthwash or gargle for inflamed gums and sore throats. Thyme essential oil is obtained from leaves and inflorescences by the method of steam distillation.

The major bioactive compounds in thyme essential oils are thymol and carvacrol (Figure 2). Thymol (named IUPAC) is a monoterpene phenol naturally derived from thyme and isomer of carvacrol, with the formula $C_{10}H_{14}O$.

Figure 1. Thyme plant



(a) (b)

Figure 2. (a) thymol, (b) carvacrol

Thymol (2-isopropyl-5-methylphenol) is found in the essential oils of thyme and oregano and has a strong medicinal, herbaceous scent. Carvacrol (5-isopropyl-2-methylphenol) is found in the essential oils of thyme, sage and oregano and has a phenolic, spicy scent. Eugenol (4-allyl-2-methoxyphenol) is also a phenol found in the essential oils of cloves, cinnamon leaves, chilli, ylang-ylang and rose. It has a spicy, pungent odor, typical of cloves.

The physical and chemical properties of phenols are: slightly acidic; very reactive; similar in action, but much stronger than alcohol.

Phenol-rich essential oils must be handled with great care. They can be toxic to the liver and irritating to the skin and mucous membranes. Phenol-rich essential oils that are irritating to the skin include cinnamon, cloves, anise oil, basil, tarragon, thyme and oregano.

Aim and objectives

The purpose of this review is to present the use of thyme extracts in diseases of the oral cavity, such as caries, gingivitis, periodontitis, oral cancer, oral candidiasis.

THERAPEUTIC PROPERTIES OF THYME

Thyme is widely used in the pharmaceutical field, mainly due to its germicidal and antiseptic properties of phenolic components.

Thymol is a biocide with strong antimicrobial properties, both used alone and in combination with other biocides, such as carvacrol. Thymol can also be used to reduce bacterial resistance to other medicines, such as penicillin. This compound also has antioxidant, anti-inflammatory, antispasmodic, anticancer, antifungal, antileishmanial, antiviral properties and potential as a growth stimulant and immunomodulator [2,3]. Nano

capsules containing thyme and thymol essential oils can be used successfully in medical practice [4].

Supercritical fluid extraction (EFS) of plant material with solvents such as CO2, propane, butane or ethylene is considered an attractive extraction method compared to conventional techniques such as steam distillation or Soxhlet extraction, as it allows the processing of plant material at temperatures reducing the contamination of the solution with solvent residues and thermal degradation [5].

Ocaña and Reglero studied thyme oils of three different species (Thymus vulgaris, Thymus zygis and Thymus hyemalis), using EFS with CO2 as solvent. The main compounds obtained were thymol, 1,8-cineole, carvacrol and borneol (Figure 3). They found that the extracts studied showed anti-inflammatory properties by reducing the release of pro-inflammatory cytokines and by increasing anti-inflammatory secretion in activated macrophages. The results suggest that essential oils from thyme extracts could be used to treat chronic diseases based on inflammatory processes.

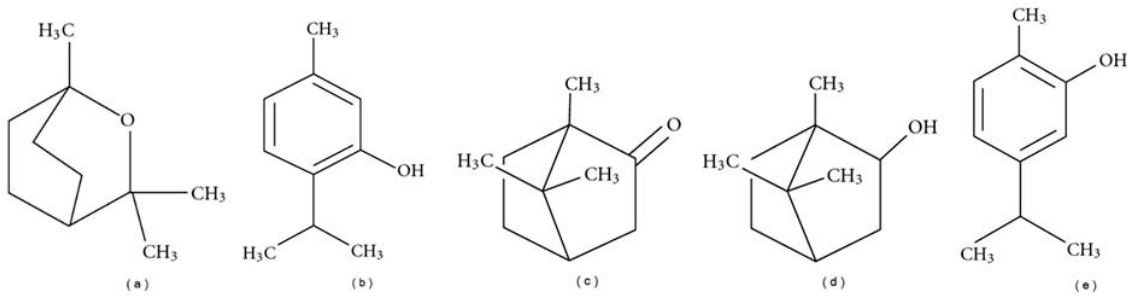


Figure 3. Chemical structures of the main compounds present in thyme extracts: (a) 1,8 cineole, (b) thymol, (c) camphor, (d) borneol, (e) carvacrol [5]

The active components of thyme glycol extract show anti-inflammatory and astringent properties that can be used in dentistry. Dental caries, periodontal disease and streptococcal pharyngitis are the most common infectious diseases in the oral cavity. Thymol appears to inhibit the growth of pathogens in the oral cavity and, in combination with other essential oils, may reduce tooth decay [6,7]. Karyogenic bacteria and periodontal bacteria are present in the dental plaque as biofilms. Thymol has membranotropic effects, the perforation of the membrane being the main mode of action of this substance [8].

Oral candidiasis can manifest as a mild or severe oral fungal infection. This infection results from the overgrowth of normally present Candida species in the oral cavity in small amounts due to predisposing factors. The structure of Candida biofilm is particularly difficult to eradicate because it is highly resistant to antifungal agents [9,10]. Various studies have shown that thyme and thymol oils, alone or in combination with antifungal drugs, have antifungal and anti-biofilm activities, and have suggested their incorporation into pharmaceutical preparations [10,11].

Studies have shown that carvacrol has a wide range of biological activities, such as antibacterial, antifungal, insecticidal, antioxidant and antitumor. The antigenotoxic potential of this monoterpene phenol has also been studied. In vitro and in vivo studies have shown the ability of carvacrol to reduce DNA damage induced by some genotoxic agents. Its ability to protect lymphocytes against DNA damage may be due to its antioxidant effects. Carvacrol acts as a free radical scavenger, which may explain its anti-mutagenic activity.

DISCUSSIONS

Fani and Kohanteb demonstrated *in vitro* antimicrobial and antifungal activity of Thymus vulgaris oil on oral pathogens: Streptococcus pyogenes, Streptococcus mutans, Candida albicans, Porphyromonas gingivalis and Aggregatibacter actinomycetem in the oral mucosa. Thyme oil, mixed with other essential oils, could be used in mouthwash, toothpaste, or aromatherapy to prevent and treat infections in the oral cavity [12].

Various studies have aimed to potentiate the antimicrobial activity of natural extracts against oral bacteria through a synergistic combination and nanoencapsulation. Lee et al. have shown that nanoencapsulation can significantly increase the synergistic antimicrobial activity of clove and thymol oil and maintain it in the oral cavity for longer [13].

Sienkiewicz et al. demonstrated that Thymus vulgaris oil inhibited the growth of strains of bacteria isolated from patients with infections of the oral cavity. Thyme essential oil has been shown to be effective against antibiotic-resistant strains of the bacteria tested [14].

Carvalho et al. aimed to evaluate the antibacterial and antibiofilm effects of essential oils and herbal toothpastes against bacteria associated with diseases of the oral cavity. The results of the study show that the essential oils of cloves, oregano, cinnamon thyme can be added to fluoride-free toothpastes to increase the inhibitory effects against bacteria from carious lesions and periodontal disease. Thyme essential oil can increase the effectiveness of chlorhexidine-containing toothpastes [15].

Studies of thyme extracts on Streptococcus mutans have shown a decrease in bacterial viability, depending on the time of action and concentration [16].

The total essential oil obtained from the aromatic plant Thymus vulgaris L. and its compounds, in particular linalool, thymol, carvacrol and their thymoquinone and thymohydroquinone derivatives, were tested *in vitro* to determine the inhibitory activity on acetylcholinesterase, thus preventing the breakdown of acetylcholine, a key clinical enzyme involved in neurodegenerative diseases. The inhibitory effect of carvacrol was 10 times stronger than that of its isomer thymol, although they have a very similar structure (Figure 1) [17].

Researchers are studying the use of herbal mouthwashes to treat oral cancer. A team of researchers from the University of Texas, San Antonio, USA, found that thymol is effective in preventing the proliferation of oral cancer cells in animals. Thymol selectively destroys cancer cells by acting on mitochondria, which produce the energy needed for cancer cells to grow. Thymol also induces apoptosis [18]. The University of Texas Health San Antonio holds a patent for thymol mouthwash to prevent oral cancer and over its mechanism of action to be used as a treatment for oral cancer.

Sertel et al. demonstrated that thyme essential oil has cytotoxic activity against squamous cell carcinoma of the head and neck [19].

Mutluay Yayla et al. conducted a study on rinsing the oral cavity with hydrosol with sage, thyme and mint tea, which resulted in attenuation of oral mucositis induced by chemotherapy [20].

Rezzoug et al. studied the chemical composition and antioxidant, antimicrobial and anticancer activities of ethanolic extracts (EE) and essential oils (EO) from two species of the Lamiaceae family, Ocimum basilicum L. and Thymus algeriensis Boiss. & Reut. The essential oils were obtained by hydrodistillation of the aerial parts of the plants and were analysed by Gas chromatography – mass spectrometry (GC-MS). Antimicrobial activity has been evaluated against several pathogens characteristic of gram-negative bacteria, gram-positive bacteria and fungi. Ethanol extracts and essential oils from both plants showed moderate antioxidant activity and moderate to weak antimicrobial activity. Anticancer activities have only been associated with EO from both plants [21].

Labib and Aldawsari set out to investigate the possibility of incorporating essential oils or active ingredients extracted from them into preparations used in the oral cavity. These preparations were evaluated for their antifungal activities, pH, viscosity, erosion and water absorption characteristics, mechanical properties, mucoadhesion, *in vitro* release behavior. The preparations showed considerable antifungal activity and acceptable physical properties [22].

Braga et al. tested the anticandidal activity of thymol, the main component of thyme oil, and eugenol, the main component of clove oil, alone or in combination, by investigating their ability to interfere with the architecture of the Candida albicans coating. Both molecules altered the morphogenesis of the cover, the effects of thymol being more pronounced than those of eugenol. Some combinations of the two molecules have led to a synergistic effect, suggesting their potentiation on inhibiting the colonization and infectivity of Candida albicans [23].

Thymol, like other ethanolic extracts of some therapeutic plants, has been studied in vital pulpotomies in children, at the teeth of the primary dentition that benefited from this therapeutic indication. Alolofi et al. they obtained promising rates of clinical and radiographic success of thymus vulgaris and propolis compared to formocresol [23].

CONCLUSIONS

Consumption of thyme in the form of flowers and leaves is safe. Caution should be exercised in the use of thyme oil, which should not be taken orally as such, but should be diluted with a diluting oil (olive or almond oil) before use.

The active components of thyme extracts show anti-inflammatory, astringent, antimicrobial, antifungal and antitumor properties that can be used successfully in dentistry. The incorporation of thyme extracts in the mouthwashes has shown a decrease in the adhesion of Streptococcus mutans to oral epithelial cells. Thymol, the main ingredient in thyme extract, is a biocide with strong antimicrobial and antitumor properties.

Identifying the active ingredients of thyme and evaluating their effectiveness in various treatments can provide useful alternatives for the development of new drugs effective in the treatment of oral diseases. There is a clear need for alternative therapies with less toxic effects.

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