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REVIEW ARTICLE

Antifungal activity of essential oils of tea tree, oregano, thyme, and cinnamon, and their components

Gustavo Aparecido Martins[1], **Julianо Lemos Bicas**[1*]

[1]Universidade Estadual de Campinas (Unicamp), Faculdade de Engenharia de Alimentos, Departamento de Ciência de Alimentos e Nutrição, Campinas/SP - Brasil

***Corresponding Author:** Juliano Lemos Bicas, Universidade Estadual de Campinas (Unicamp), Faculdade de Engenharia de Alimentos, Departamento de Ciência de Alimentos e Nutrição, Rua Monteiro Lobato, 80, CEP: 13083-862, Campinas/SP - Brasil, e-mail: bicas@unicamp.br

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Abstract

Phytopathogenic fungi are responsible for sizeable postharvest food losses. The traditional form of controlling these fungi is related to synthetic antifungals. However, the emergence of resistant strains and their high cost, among other problems, encourage the scientific community to seek alternatives in natural substances at a lower cost. In this scenario, a group that stands out among these natural substances is essential oils. Essential oils are naturally volatile and aromatic compounds derived from plants. These compounds have bactericidal, virucidal, insecticidal, anti-inflammatory, antioxidant, and antifungal properties. This review presents the essential oils of tea tree, oregano, thyme, and cinnamon and their main components identified as responsible for their antifungal activity.

Keywords: natural; volatile; postharvest; GRAS; bioactive; pesticide; rot; aromatic; synthetic.

Highlights

- Interest in natural substances to replace conventional antifungals is growing
- Essential oils are potential substitutes for conventional antifungals
- Mechanism of action: perforate cell wall, disrupt hyphae, and liquefy cell membranes

1 Introduction

Food loss and waste are global problems throughout the production chain. Fruits and vegetables represent 40% to 50% of world losses, with 54% occurring during the production, postharvest, handling, and storage stages. In Latin America, approximately 30% of fruits and vegetables are lost (Santos et al., 2020).

The loss of approximately 40% of the world's food production is caused by animals, weeds, and pathogens. The most significant impact on horticultural losses is postharvest diseases caused by bacteria and fungi that cause rot, seeing that the fruits are the group related to the greatest losses (Matrose et al., 2021).

Phytopathogenic fungi are responsible for approximately 85% of postharvest diseases that affect fruits. Some of the genera most commonly associated with fruit diseases are *Alternaria, Aspergillus, Botrytis, Colletotrichum, Diplodia, Monilinia, Penicillium, Phomopsis, Rhizopus,* and *Mucor*. Among these, the genus *Botrytis* stands out for having already been recognized as the most disastrous for fresh fruits and vegetables (Matrose et al., 2021).

Botrytis cinerea causes gray rot, characterized by soft gray spots on leaves, stems, flowers, and fruits, such as strawberries, grapes, apples, and cherries, among others (Matrose et al., 2021). The conidia of *B. cinerea* attach to the surface of the host through weak hydrophobic interactions. After germination of the conidia, the fungus attaches more strongly to the surface. *B. cinerea* can penetrate tissues and induce programmed cell death due to the production of toxins, oxalic acid, and reactive oxygen species (Roca-Couso et al., 2021).

Green and blue rots are caused by the genus *Penicillium*, which mainly affects citrus fruits. *Penicillium* species form conidia that invade fruits through wounds. The infection begins with the appearance of a soft area around the wound and a white mycelium that produces conidia. The decomposition of the fruit occurs in a few days. In the final phase, the fruit is covered with blue or green conidia, depending on the infecting species (Hammami et al., 2022).

In addition to postharvest diseases, fungi can also cause plant diseases, such as anthracnose, leading to loss of crop productivity and quality (Jain et al., 2019). The genus *Colletotrichum* is famous for causing anthracnose. This disease mainly affects fruits such as bananas, papayas, mangoes, avocados, and dragon fruit and infects leaves, flowers, twigs, and branches. Infection occurs during the flowering and fruiting stages, the main symptoms being dark lesions, which can merge with conidia on the fruit surface (Zakaria, 2021).

Witches' broom (caused by the fungus *Moniliophthora perniciosa*) is one of the primary diseases of cacao (Lisboa et al., 2020). It has a tremendous economic and social impact due to the severe impacts on cocoa and chocolate production (Andrade Silva et al., 2020). During the 1970s, it was responsible for losing more than 90% of cocoa production in Rondônia state in Brazil (Lisboa et al., 2020).

The control of phytopathogenic and spoilage fungi has traditionally been carried out using synthetic antifungals (Jiménez-Reyes et al., 2019). They are recognized for suppressing the development of diseases in fruits and vegetables. However, the continuous use of these substances has caused significant problems, such as the emergence of resistant postharvest pathogen strains (Matrose et al., 2021). Thus, the need for tools to prevent the proliferation of undesirable fungi in the agro-food chain becomes evident.

Plants produce a wide diversity of molecules, especially secondary metabolites, such as essential oils. These oils and their volatile components are critical for defending plants against pests and diseases and are also crucial in plant-plant interactions and for attracting insects that disperse pollens and seeds (Ebadollahi et al., 2020; Nazzaro et al., 2017; Raveau et al., 2020).

More than 3,000 essential oils have already been identified, consisting of a rich mixture of bioactive compounds of different classes, mostly terpenes and terpenoids. Essential oils are recognized sources of compounds presenting different biological properties, such as antibacterial, insecticidal, fungicidal, nematicidal, herbicide, antioxidant, and anti-inflammatory activities (Falleh et al., 2020; Raveau et al., 2020). They commonly have GRAS (Generally Recognized as Safe) status, making essential oils potential natural preservatives and antifungals for application in the agri-food chain (Nazzaro et al., 2017; Pandey et al., 2017).

The following section presents a brief history of conventional antifungals, some classes, and disadvantages associated with their application. In a second moment, this text addresses the potential use of some essential oils and their main components as an alternative to synthetic antifungals.

2 Methodology

This literature review focused on the potential for replacing classic antifungals with essential oils. Thus, a detailed search was conducted on several websites and databases such as Google Scholar, SciELO, Scopus, and ScienceDirect, among others, thus priorizing studies from the last ten years. The main search terms were antifungal, pesticide, essential oil, mechanism, history, postharvest, and components.

3 Conventional antifungal agents

3.1 History of conventional antifungal

Since ancient times, simple inorganic salts have been used as plant pesticides. In 1885, it was discovered that copper sulfate and lime could control specific diseases, such as potato late blight. From that moment on, interest in the chemical control of diseases emerged (Russell, 2005). Until around 1940, antifungals focused on diseases that affect fruits, vegetables, and seeds, and antifungals were prepared by users based on essential recipes (Morton & Staub, 2008). The use of synthetic compounds began in 1934 with dithiocarbamates (Thind, 2021).

Between 1940 and 1970, dithiocarbamates became the most widely used group of antifungals, as they were more active, less phytotoxic, and more easily prepared by the user. During this period, new classes of antifungals emerged, such as phthalimides, triazines, and dinitroanilines. Especially between the 1960s and 1970s, there was a rapid growth in research, development, and the market for antifungals, when mancozeb and chlorothalonil, the most widely used protective antifungals, appeared, in addition to thiabendazole, and the systemic treatment of carboxin seeds (Morton & Staub, 2008). In the 1960s, the first fungicides appeared that inhibited a specific target site (Hirooka & Ishii, 2013).

From the 1970s onwards, most fungicides developed were systemic in nature, acting internally to eradicate infections, having a specific site of action, and applied in smaller quantities. Between 1970 and 2000, the main classes were organophosphates, phenylcarbamates, dicarboximides, and sterol inhibitor fungicides (Hahn, 2014). In recent decades, to prevent fungi from developing resistance to pesticides, they have been created with two modes of action, generally site-specific action and multisite inhibitors (Thind, 2021). Some classes of conventional antifungals, such as triazoles, phenylpyrroles, strobilurins, benzimidazoles, and morpholines, are discussed below.

3.2 Classes and mechanism of action

Over the years, several antifungals were created and divided into several classes. Some of the main classes of synthetic antifungals are triazoles, phenylpyrroles, and strobilurins (Baibakova et al., 2019).

Triazoles are the largest class of antifungals. The first commercially sold triazole was triadimefon, launched by Bayer in 1973 (Morton & Staub, 2008). Other representatives of this class are tebuconazole, prothioconazole, difenoconazole, cyproconazole and propiconazole. The mechanism of action of triazoles is based on the inhibition of ergosterol synthesis and blocking of the P450-dependent enzyme (CYP 51) (Matin et al., 2022), which are essential constituents of the plasma membrane that preserve its fluidity and barrier function under different environmental conditions (Menon, 2018).

Antifungals of this class are used against fruit and vegetable pathogens. Some genera of fungi that can be controlled with them are *Botrytis*, *Ustilago*, *Cercospora*, *Tilletia Zymoseptoria*, *Fusarium*, *Cochliobolus*, *Erysiphe*, *Altemaria*, *Puccinia*, *Septoria*, *Pythium*, *Drechslera*, *Pyrenophora*, *Rhynchosporium*, and *Cladosporium* (Baibakova et al., 2019). The disadvantage of triazoles is that their systematic use leads to the emergence of resistant strains. Some mechanisms associated with resistance are mutations in the CYP51 gene mutations in the promoter region leading, that is, to overexpression of CYP51. Some phytopathogens that have already had resistance reported are *Rhynchosporium commune*, *Sclerotinia homoeocarpa*, *Venturia inaequalis*, and *Zymoseptoria tritici* (Poloni et al., 2021).

The phenylpyrroles class has fludioxonil as the only representative in the United States of America (USA) and European markets, having been introduced in 1993 and 2008, respectively (Apell et al., 2019). The use of phenylpyrroles presents a low risk of the emergence of resistant strains, as it is a non-systemic molecule that inhibits spore germination, germ-tube elongation, and mycelial growth. However, they may present phytotoxicity, reducing CO_2 assimilation, transpiration, and stomatal conductance (Baibakova et al., 2019; Geetha, 2019). Some genera of fungi that can be controlled with its use are *Botrytis*, *Fusarium*, *Magnaporthe*, *Aspergillus*, *Monilinia*, and *Penicillium* (Bersching & Jacob, 2021).

In 1996, strobilurins, effective and broad-spectrum antifungal agents suitable for various crops, were launched and popularly used in cereals and are still widely used today to control pathogens in soybeans, rice, cereals, vegetables, fruit trees, among other plants. In 2014, azoxystrobin and pyraclostrobin were the best-selling fungicides (Morton & Staub, 2008; Wang et al., 2021). Some representatives of this class are azoxystrobin, pyraclostrobin, trifloxystrobin, fluoxastrobin, picoxystrobin, and kresoxim-methyl (Zhang et al., 2020).

Strobilurin's mechanism of action consists of inhibiting mitochondrial respiration by connecting to the external site of cytochrome bc1, preventing the exchange of electrons between cytochromes b and c. This causes a cell energy deficit, resulting in stasis (Shcherbakova, 2019). They are used against *Puccinia*, *Septoria*, *Alternaria*, *Cladosporium*, *Epicoccum*, *Botrytis*, *Rhynchosporium*, *Fusarium*, and *Rhizoctonia* (Baibakova et al., 2019). The emergence of resistant strains has already been reported. Resistance can occur for two reasons: changes in the mitochondrial gene cytochrome b (CYTB), altering the peptide sequence, which prevents the binding of fungicides, or it can be due to a deviation in mitochondrial electron transfer, avoiding the inhibitory site in the cytochrome bc1 (Sánchez-Torres, 2021).

In addition to the already mentioned problem of the emergence of strains resistant to conventional antifungals, other disadvantages associated with their use are toxic residues in plants and fruits, possible intoxication and infertility associated with handling, persistence for many years in the environment without degrading, and high cost, approximately 20% of the production cost is allocated to antifungals (Jiménez-Reyes et al., 2019).

Given this scenario, the scientific community's interest is directed toward searching for new substances capable of controlling pathogenic diseases (Zhou et al., 2014). Considered relatively safe and environmentally friendly, natural antimicrobial substances have proven to be potential substitutes for synthetic antifungals. However, more research is needed to understand their mechanisms of action and analyze their effectiveness (Moraes Bazioli et al., 2019).

Among these natural substances, a group that stands out is essential oils, which will be further discussed in the next section. These essential oils can be extracted from various plants and have the potential as substitutes for synthetic antifungal agents due to their ability to inhibit a variety of pathogens and, in addition, are harmless to humans at the commonly used dosage (Kong et al., 2019; Park et al., 2009).

4 Essential oils

Essential oils are natural volatile oils, aromatic from plants, obtained from flowers, roots, seeds, leaves, and bark. They are lipophilic secondary metabolites and important plant defense mechanisms (An et al., 2019). Its composition is quite varied, resulting from the mixture of several chemical classes, such as monoterpenes, sesquiterpenes, aliphatic alcohols, ketones, aldehydes, acids, and simple benzenoids (Nahar et al., 2021).

Essential oils can be obtained in several ways, with the characteristics and components of the oil being the determining factor for choosing the extraction technique. These techniques can be divided into two groups, classical methods, such as hydrodistillation, steam distillation, hydro diffusion, and liquid-liquid extraction, and emerging methods, such as supercritical fluid extraction, subcritical liquid extraction, and solventless microwave extraction. Emerging methods have demonstrated greater extraction efficiency in the time required for oil isolation, energy dissipation, yield, and quality (Aziz et al., 2018).

In recent years, essential oils have aroused great interest in the most varied areas due to their bactericidal, virucidal, insecticidal, anti-inflammatory, antioxidant, and antifungal properties. The latter is mainly due to its potential substitute for synthetic antifungals (Angane et al., 2022; Kong et al., 2019; Park et al., 2009).

The antifungal activity of essential oils is constantly associated with their volatile bioactive components, their interaction with the plasma membrane, and their disruption of mitochondrial functions. They can break the plasma membrane and make it more permeable (Mutlu-Ingok et al., 2020). This mechanism occurs through a permeabilization process, where essential oils penetrate and break the membrane and cell wall of fungi (Tariq et al., 2019).

Furthermore, essential oils can interrupt ion transport processes, interact with membrane proteins, and affect the functioning of enzymes by interacting with their active site (Mutlu-Ingok et al., 2020). In yeast, they damage the cell wall by establishing a membrane potential and interrupting ATP production (Tariq et al., 2019).

The European Commission 2008 released a constantly updated list, including components of essential oils with approved use in food as food additives. Among the registered compounds that do not pose a risk to human health are carvone, eugenol, limonene, linalool, pinene, thymol, carvacrol, vanillin, citral, cinnamaldehyde and menthol. Some of these compounds will be discussed in the next section. The United States Food and Drug Administration (FDA) also recognizes these compounds as "generally recognized as safe" (GRAS) (Angane et al., 2022). Figure 1 presents the chemical structure of some of these components of essential oils.

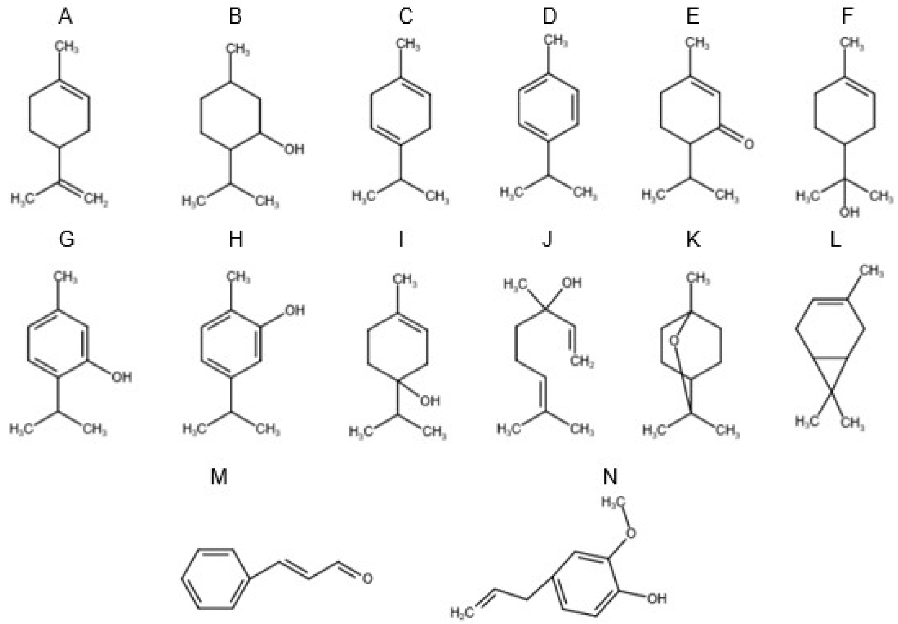

Figure 1. Chemical structures of limonene (A), menthol (B), γ-terpineol (C), p-cymene (D), piperitone (E), α-terpineol (F), thymol (G), carvacrol (H), terpinen-4-ol (I), linalool (J), 1,8-cineol (K), 3-carene (L), cinnamaldehyde (M), eugenol (N). Source: Authors (2023).

However, it is worth mentioning that essential oils are not exempt from possible adverse effects. Some of them can cause allergies, dermatitis, stomatitis, kidney irritation, and alterations in the intestinal mucosa. These effects are directly related to the dose, mode of administration, the health status of the person, additives in oils, and their composition (D'agostino et al., 2019).

Essential oils have been used as alternatives to conventional antifungals. Usually, the antifungal activity results from the action of their major compounds (Perricone et al., 2015) (as discussed in section 5), although minor components also play essential roles, such as facilitating oil penetration into the cell, through disruption and/or membrane permeabilization (D'agostino et al., 2019; Perricone et al., 2015). In some instances, the isolated components of the essential oil have even better antifungal activity than the oil (Hou et al., 2022), while it has already been verified that synergism might occur between specific essential oil components in a way that the activity of a mixture is more active than the individual activities (D'agostino et al., 2019).

Some examples of essential oils can be seen in Table 1. The following section will present some of the most studied essential oils in recent years and what is known about some of the components of these oils, which can also have antifungal action individually. Next, some of the most studied essential oils in recent years will be presented, some of their characteristics, principal components, and results obtained in recent studies on their action on some of the previously mentioned pathogenic fungi. In section 5, some of the main components of these essential oils identified as responsible for their antifungal action will be further discussed. Table 2 shows the components of the oils, which will be discussed, found in higher concentrations in different studies.

Table 1. Essential oils, main components with antifungal activity, and related fungi.

Essential oils	Main components	Fungus	References
Cinnamon	cinnamaldehyde	*Phytophthora colocasiae*	Hong et al. (2021)
Cumin	cuminaldehyde, p-cymene, γ-terpinene 1,8-cineol	*Fusarium sp*	Kedia et al. (2014)
		Aspergillus sp	
Clove	1,8-cineole, eugenol	*Alternaria brassicae*	Diánez et al. (2018)
		Fusarium oxysporum	
Eucalyptus	p-cymene, 1,8-cineole	*Aspergillus niger*	Bardaweel et al. (2014)
		Aspergillus flavus	
Pepper mint	linalool, menthol, piperitone	*Aspergillus niger*	Mahboubi & Haghi (2008)
Wild orange	α-terpineol, terpinen-4-ol, linalool, limonene	*Penicillium digitatum*	Trabelsi et al. (2016)
		Penicillium italicum	
Oregano	thymol, carvacrol	*Botrytis cinerea*	Daferera et al. (2003)
		Fusarium sp	
		Penicillium digitatum	Vitoratos et al. (2013)
		Penicillium italicum	
		Aspergillus flavus	Manso et al. (2011)
Tea tree	terpinen-4-ol, 3-carene, α-terpineol	*Botrytis cinerea*	Cheng & Shao (2011)
		Penicillium italicum	
		Penicillium digitatum	
		Colletotrichum acutatum	
		Aspergillus niger	An et al. (2019)
		Aspergillus ochraceus	Kong et al. (2019)
Thyme	thymol, carvacrol, p-cymene	*Fusarium sp*	Daferera et al. (2003)
		Aspergillus sp	Segvić Klarić et al. (2007)
		Penicillium sp	
		Cladosporum sp	
		Botrytis cinerea	Banani et al. (2018)
		Alternaria brassicae	Diánez et al. (2018)
		Fusarium oxysporum	
		Penicillium italicum	Vitoratos et al. (2013)
		Penicillium digitatum	

Table 2. Essential oils, main components, and relative content determined by Gas Chromatography-Mass Spectrometry (CG-MS).

Essential oils	Main components	Relative content (%)		
		Kulkarni et al. (2012)	Lee et al. (2013)	Vázquez et al. (2023)
Tea tree	terpene-4-ol	48.70	47.31	38.42
	γ-terpinene	10.40	20.59	16.58
	α-terpineol	2.00	3.020	4.66
		Akkaoui et al. (2020)	Petrakis et al. (2023)	Xie et al. (2019)
Oregano	carvacrol	32.36	77.33	58.13
	p-cymene	16.25	9.64	17.85
	timol	12.06	1.30	8.15
		Cutillas et al. (2018)	Hudaib et al. (2002)	Khan et al. (2019)
Thyme	timol	50.30	42.75	60.55
	γ-terpinene	8.30	18.01	9.48
	p-cymene	19.40	16.04	8.55
		Ainane et al. (2019)	Bisht et al. (2021)	Yu et al. (2020)
Cinnamon	cinnamaldehyde	89.31	40.60	73.35
	linalool	1.60	10.20	10.61
	cinnamyl acetate	2.44	19.60	8.58

4.1 Tea tree oil

Tea tree oil (TTO) is a clear/pale yellow oil with a pleasant odor obtained by distillation of the leaves and terminal branches of *Melaleuca alternifolia* Cheel, a plant native to Australia that does not occur naturally anywhere else in the world (Carson et al., 2006; Yue et al., 2020).

This oil has been widely used by the medicinal and cosmetic industries to treat inflammation, headaches, colds, and coughs. It has even been suggested to prevent acne by reducing inflammation in the skin, and its antitumor activity against breast cancer cells has also been reported *in vitro* tests (An et al., 2019). However, it has also been reported that this oil can cause allergies and irritations, especially when deteriorated or poorly preserved (D'agostino et al., 2019).

TTO is used as an antifungal, antibacterial, antiviral, antioxidant, anti-inflammatory, and anticancer agent (Carson et al., 2006; Yue et al., 2020). This oil has already shown a satisfactory inhibitory effect against black mold, a postharvest disease caused by *A. niger* (An et al., 2019). *In vivo* tests also showed that TTO can prevent rot caused by *A. ochraceus* in grapes (Kong et al., 2019).

In recent studies, the composition of TTO was determined using gas chromatography (GC) and gas chromatography coupled to mass spectrometry (GC-MS), through which the compounds present in this oil were identified. Table 2 shows the components found in higher concentrations (An et al., 2019; Kong et al., 2019).

Among the main components of TTO, terpinen-4-ol and α-terpineol were identified as antifungal compounds capable of inhibiting mycelium growth and spore germination, being the main contributors to the antifungal activity of the oil (An et al., 2019; Kong et al., 2019). These components individually show a superior destructive effect than TTO on the morphology of hyphae, spores, and plasma membrane (An et al., 2019).

4.2 Oregano essential oil

Oregano (*Origanum vulgare* L.) is a shrub native to southern Europe and western Asia. In Brazil, it is found mainly in the South and Southeast regions. The essential oil of *O. vulgare* is characterized by having a high content of phenolics and is also composed of monoterpene hydrocarbons, sesquiterpenes, and oxygenated monoterpenes (Paulo et al., 2021). Essential oil extraction is traditionally performed by steam distillation of leaves or buds but can also occur by hydrodistillation, CO_2 extraction, and supercritical fluid extraction.

This oil is commonly used by the fragrance, pharmaceutical, food, and aroma industries (Bounar et al., 2020) and is a recognized antifungal, antioxidant, anti-inflammatory, and anti-diabetes agent. Furthermore, its effectiveness against food-deteriorating bacteria has been highlighted in many studies (D'agostino et al., 2019). However, there are certain limitations regarding its use since it is degraded when exposed to high temperatures, pressure, light, and oxygen during food processing and can alter sensory characteristics depending on the concentration used (Paulo et al., 2021).

The antifungal activity of oregano essential oil has already been verified against the most varied microorganisms, such as *B. cinerea*, *Penicillium italicum*, *and P. digitatum* (Vitoratos et al., 2013). Such activity is related to specific components of this oil, such as carvacrol and thymol, that is their main active compounds (Paulo et al., 2021). Table 2 shows the components found in greater quantities in *O. vulgare* oil in different studies.

This oil proved to be an effective fungicide against some *Fusarium* species, with a minimum inhibitory concentration (MIC) ranging from 0.156 to 0.078 μL/mL, the lowest of which was able to inhibit the development of *F. culmorum*, *F. equiseti*, *F. avenaceum* and *F. moniliforme* (Bounar et al., 2020).

Studies have evaluated the combined antifungal activity of oregano oil with other essential oils. The combination with thyme essential oil, at a concentration of 0.078 μL/mL, completely inhibited the germination of spores from different *Fusarium* species. In *in vivo* tests conducted on potatoes contaminated with *Fusarium* species, the combination of these oils showed a more significant inhibitory effect than the separate oils (Bounar et al., 2020). It was also reported that the combination of oregano extract, thyme essential oil, and peppermint stimulated the growth of probiotic bacteria and positively affected the gut's microbial composition (Angane et al., 2022).

4.3 Thyme essential oil

Thyme (*Thymus vulgaris* L.) is a grass of the Lamiaceae family found worldwide, mainly in southern Europe (Allahverdiyev et al., 2013; Jakiemiu et al., 2010). Its essential oil is obtained by steam distillation of the aerial parts of the plant. It has a spicy aromatic odor, and color can vary from yellow to dark reddish-brown (Evans & Evans, 2009).

Studies have already reported that this essential oil has antifungal, antibacterial, antiparasitic, and antiviral activity, thus being widely used in traditional medicine as an anti-inflammatory, antiviral, antibacterial, and antiseptic agent (Kowalczyk et al., 2020). In the food industry, its use is related to its antibacterial, antifungal, and antioxidant activity (Nieto, 2020).

Table 2 shows the components found in the highest concentration in thyme essential oil, determined by GC and GC-MS, in different studies. The oil was obtained from thyme grown outdoors in the city of Ravenna, Italy. Some of the main components of this oil are thymol, γ-terpinene, p-cymene, carvacrol, and linalool (Satyal et al., 2016), with thymol and carvacrol being mainly responsible for its antifungal activity (Shabnum & Wagay, 2011).

The antifungal activity of thyme oil has been proven against various microorganisms. It reduced the diameter of wounds caused by *B. cinerea*, the fungus responsible for gray mold, in experiments conducted on apples (Banani et al., 2018). It presented an ED50 (dose that inhibits 50% of mycelial growth) of 677 µL/mL against *A. brassicae* and 363 µL/mL against the pathogenic fungus *F. oxysporum* (Diánez et al., 2018).

In recent studies, thyme essential oil has been shown to be a potential substitute for nitrite as an antioxidant in meat (Blanco-Lizarazo et al., 2017) and also as a preservative in hamburgers (Radünz et al., 2020). Adding thyme oil also delayed the deterioration of minced pork during 15-day refrigerated storage (Boskovic et al., 2017).

4.4 Cinnamon essential oil

Cinnamon is a spice obtained from trees in the Lauraceae family. It is mainly found in Southeast Asia, with China being the world's largest producer of cinnamon. Its oil is industrially obtained by steam distillation (Yu et al., 2020). It has a yellowish color, cinnamon odor, and spicy burnt taste (Burdock, 2010).

Cinnamon essential oil is used as a food additive, condiment, and flavor due to its antioxidant and preservative properties. It is also used medicinally in certain countries, such as China and India (Yu et al., 2020). Cinnamaldehyde is one of the most active components of this oil that contributes to its biological activities (Shreaz et al., 2016) and can be used to prevent food spoilage and is a potential substitute for synthetic preservatives (Sun et al., 2020). Cinnamaldehyde will be discussed further in section 5.5. Table 2 shows the components found in the highest concentration of cinnamon essential oil, determined by GC-MS, in different studies.

Cinnamon essential oil significantly inhibited mycelial growth, spore viability, and germination of *P. colocasiae* in yam leaves and shoots. At a concentration of 0.625 mg/mL, the maximum inhibition of mycelial growth (100%), zoospore germination (100%), and fungus sporulation (85.26%) was achieved (Hong et al., 2021).

5 Main components of essential oils are responsible for their antifungal action

In this section, some of the main components of the essential oils presented in section 4, identified as responsible for their antifungal action, will be presented. These components are α-terpineol, terpinen-4-ol, carvacrol, thymol, and cinnamaldehyde.

5.1 α-TERPINEOL

The α-terpineol (Figure 1F) is a cyclic monoterpene ($C_{10}H_{18}O$, MM = 154.25 g/mol), which has two enantiomers, the R-(+)-α-terpineol, which has a floral aroma and is widely found in nature and S-(-)-α-terpineol, which has an aroma reminiscent of pine and is rarer than other aromas (Boelens & van Gemert, 1993; Sales et al., 2020).

Even though it is found in various plants, this compound is obtained mainly through chemical synthesis. The most classic method consists of hydrating crude oil with α-pinene or turpentine, but other methods with

3-carene, limonene, pinene, and pentane tricarboxylic acid are also used. α-terpineol can still be obtained by biochemical methods through the biotransformation of limonene, α- and β-pinene (Sales et al., 2020).

This monoterpene is used as a fragrance in the cosmetics industry (perfumes, body lotions) and as an aroma (beverages, confectionery, and condiments) by the food industry. In addition, it has excellent potential for application due to its antioxidant, anti-inflammatory, anticonvulsant, antimicrobial, anticancer, antifungal, and antihypertensive properties and because it is considered a potent inhibitor of superoxide production (Khaleel et al., 2018; Sales et al., 2020).

The antifungal activity of α-terpineol has already been reported in several studies, such as, for example, in the fight against sour rot, according to the study of Zhou et al. (2014) which determined the MIC and CFM values of a-terpineol to be 2.00 and 4.00 µL/mL, respectively, and the mycelial growth of *Geotrichum citri-aurantii* was wholly inhibited at a concentration of 2.00 µL/mL. However, at 0.25 and 0.50 µL/mL concentrations, the mycelial growth of *G. citri-aurantii* was slightly stimulated.

The study suggests that α-terpineol can act on the cell membrane structure of *G. citri-aurantii* and compromise its integrity. This occurs because the tests carried out with α-terpineol showed a more excellent extracellular conductivity, lower extracellular pH, and a decrease in the total lipid content of the cells compared to the control. These results indicated irreversible damage to the cytoplasmic membranes of *G. citri-aurantii* because the lower pH and the decrease in lipid content indicate the extravasation of protons and intracellular components. Furthermore, it was observed that the hyphae were shrunken and distorted after exposure to α-terpineol (Zhou et al., 2014).

In another study, α-terpineol was pointed out as the main component of *M. alternifolia* oil responsible for the inhibition of *A. ochraceus*, being the one that causes the most significant suppression of mycelial growth, spore germination, and membrane destruction. At a concentration of 0.4 µL/mL, α-terpineol showed a rate of inhibition of mycelial growth of 50.4% and a rate of inhibition of spore germination of 49.0%. At concentrations of 0.8 and 1.6 µL/mL, it blocked hyphal growth and spore germination for 7 days. Furthermore, it inhibited the growth of *A. ochraceus* in grapes incubated at 25 °C for 7 days (Kong et al., 2019).

Kong et al. (2019) observed that *A. ochraceus* undergoes a series of changes when exposed to α-terpineol. Their hyphae become rough and fractured, which leads to leakage of their contents and inhibition of mycelial growth. Cytoplasms became irregular and degenerated, with large empty holes. These changes were attributed to blocking the synthesis of the cell wall, cytomembrane, cytoplasm, and organelles, thus affecting the growth and morphology of fungi and spores.

In the study by An et al. (2019), the antifungal activity of α-terpineol was also related to damage to cell walls, membranes, and cytoplasm. In that study, a higher electrical conductivity was also reported in the group treated with α-terpineol than in the control group. All mycelium exposed to α-terpineol became twisted, broken, wrinkled, coarse, and with reduced cytoplasmic content. The sporangia were also affected, being badly broken. In *in vivo* tests, it completely inhibited the growth of *A. niger* in grapes incubated at 25 °C for 7 days.

5.2 Terpinen-4-ol

Terpinen-4-ol (Figure 1I), like α-terpineol, is a monoterpene that has two stereoisomers, R-(−)-terpinen-4-ol and S-(+)-terpinen-4-ol. Its aroma is spicy and clayey, with a woody touch (Carneiro Neto et al., 2022).

In their study, Kong et al. (2019) identified terpinen-4-ol as the second principal component of *M. alternifolia* oil responsible for inhibiting *A. ochraceus*. The study caused morphological changes in hyphae and deformed *A. ochraceus* spores, inhibiting their mycelial growth.

Seven days after treatment, using a concentration of 0.8 µL/mL, its mycelial growth inhibition rate was 69.6%, and the spore germination inhibition rate was 68.0%. At a 1.6 µL/mL concentration, there was an almost complete blockage of mycelial growth and spore germination. In grapes treated with terpinen-4-ol, the incidence of the disease was 45% (Kong et al., 2019).

Exposure to terpinen-4-ol caused a series of alterations in *A. ochraceus*, such as a reduction in electrical conductivity, disruption and thinning of hyphae, and irregular and degenerated cytoplasm. These changes were attributed to blocking the synthesis of the cell wall, cytomembrane, cytoplasm, and organelles, thus affecting the growth and morphology of fungi and spores (Kong et al., 2019).

Similar results were obtained in a study conducted with *A. niger*. In this study, the antifungal activity of terpinen-4-ol was associated with its ability to disrupt cell walls, membranes, and cytoplasm. Its application reduced the incidence of black mold in grapes to 27% compared to the control (An et al., 2019).

In this study, once again, terpinen-4-ol showed higher electrical conductivity than the control group, suggesting its effectiveness in destroying the membrane permeability of *A. niger*. Furthermore, it also seriously fractured the hyphae, which led to leakage of contents, damaged cell walls, and made the sporangia small and ruptured (An et al., 2019).

5.3 Carvacrol

Carvacrol (2-methyl-5-(1-methylethyl)phenol, (Figure 1H) is a phenolic monoterpene ($C_{10}H_{14}O$), which has an isomer, thymol. Its odor is spicy and reminiscent of oregano (Lima et al., 2017). It is considered non-toxic to humans and is commonly used as a flavoring agent (Chaillot et al., 2015).

Carvacrol can be obtained by extracting it directly from plants such as oregano (*O. vulgare*), thyme (*T. vulgaris*), pepper (*Lepidium flavum* Torr.), and black cumin (*Nigella sativa* L.). However, it can also be synthesized chemically and biochemically. It is recognized for its antiviral, antibacterial, antifungal, anti-inflammatory, and antioxidant activity (Bayir et al., 2019).

Over the years, several mechanisms of action have been suggested to explain the antifungal activity of carvacrol. It has already been pointed out that this monoterpene disrupts and depolarizes the plasma membrane, thus targeting membrane proteins. In a study with *Candida albicans*, it demonstrated the ability to fragment the endoplasmic reticulum, causing disruption of its organization and unfolding of the protein response, by activating genes involved in proteolysis, amino acid metabolism, and phospholipid translocation (D'agostino et al., 2019).

5.4 Thymol

Thymol (5-methyl-2-(1-methylethyl)phenol, (Figure 1G) is a phenolic monoterpene ($C_{10}H_{14}O$) isomer of carvacrol. It has a white crystalline color and a characteristic pleasant odor. It has good solubility in organic solvents but is poorly soluble in water (Lima et al., 2017). Several studies have proven its antifungal activity, although its mechanisms are still not entirely clear (D'agostino et al., 2019).

In a study with *F. graminearum*, thymol decreased the production and germination of conidia, damaged the plasma membrane, causing electrolyte leakage, and mainly affected the hyphae, which is a high concentration collapsed and broke, reaching a wholly inhibited growth (Gao et al., 2016).

Synergistic effects between thymol and other fungicides have been previously reported. Together with fluconazole, thymol showed a synergistic effect against *Trichophyton rubrum* and *A. fumigatus*. In a study with *C. albicans, C. krusei*, and *C. glabrata*, a synergistic effect was also reported when combined with fluconazole. Other synergistic interactions were observed when combined with itraconazole against *Pythium insidiosum* and nystatin against *Candida* spp. (D'agostino et al., 2019).

5.5 Cinnamaldehyde

Cinnamaldehyde (3-phenylprop-2-enal, (Figure 1M) is a yellowish liquid with a strong cinnamon odor and insoluble in water and miscible in vegetable oils and ethanol. It is found in cinnamon and its leaf, leaf from cassia, and lemon balm. It can be obtained both by extraction and by chemical synthesis. The latter occurs by condensing benzaldehyde with acetaldehyde in the presence of sodium or calcium hydroxide (Burdock, 2010).

In *in vitro* tests, cinnamaldehyde has already been shown to be effective against *A. niger*, with its antifungal effect directly linked to the dose and form of treatment. In doses greater than 150 μg/mL, the growth of *A.*

niger was insignificant, and the liquid treatment was the most effective. Its antifungal activity has been associated with its ability to alter the morphology and ultrastructure of hyphae, loss of cytoplasm, and destruction of organelles (Sun et al., 2020).

Against *G. citri-aurantii*, cinnamaldehyde made the hyphae distorted, shriveled, and crushed and caused a structural disorder of the cytoplasm. Its antifungal activity was not associated with damage to the plasma membrane but to the cell wall, something supported by the reduction in chitin content and increased activity of AKP, an enzyme produced in the cytoplasm that is released by fungal cells that have damage to their wall cell (OuYang et al., 2019).

6 Final considerations

Phytopathogenic fungi constitute a significant challenge for agriculture, being responsible for nutritional, color, texture, physiological, and biochemical changes in various foods, causing significant economic losses and losses of food products.

Since the 1930s, several synthetic antifungals have been developed aiming to control these fungi, such as triazoles, phenylpyrroles, strobilurins, benzimidazoles, and morpholines, among others. However, concern has been growing regarding using these synthetic antifungals due to the emergence of resistant strains, toxic residues in food, and long-term persistence in the environment without being degraded, among others.

In this scenario, there is growing interest in research into natural substances with antifungal activity, such as extracts, essential oils, or active plant compounds. Recent studies demonstrated that essential oils are potential substitutes due to their ability to pierce the cell wall, break hyphae, liquefy cell membranes, and affect the functioning of enzymes, preventing the development of fungi.

The major challenge associated with the applicability of essential oils is the volatility of specific compounds, making it difficult to verify the effects of a volatile compound in a matrix due to the short interaction time between them. A potential solution to this problem is using encapsulation techniques, such as microencapsulation and nanoemulsions. They significantly reduce volatility, increase stability, shelf life, and preserve biological activity.

Essential oils are an interesting alternative to conventional antifungals. It is expected that scientific and technological development in this sector will allow the large-scale replacement of conventional antifungals with formulations containing essential oils. However, until this scenario becomes a reality, research on this topic must be encouraged, aiming to discover the main components of these oils responsible for their antifungal activity, understand the mechanisms of action and develop techniques to enable the interaction between them and the matrix.

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