The Essential Volatile Oils for the Treatment of Candida infections

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ABSTRACT:
The use of plant extracts and especially essential oils is a traditional medicine method that is many centuries and even millennia old. We summarized and analyzed the effects of some essential oils or their extracts on Candida fungal strains and the methods used in testing antifungal in laboratories. The use of such essential oils in laboratory experiments showed considerable therapeutic results and antifungal effects on different Candida strains. The modern medicine, reconsider it in order to use it as an alternative to the antimonyocyte medication in fungal infections. The newest research demonstrated that these natural origin substances can be used with success in many cases of fungal infections.

Keyword: essential oils, fungal infections, Candida species, natural origin antifungal.

INTRODUCTION
Candida infections are the most frequent fungal infections in human pathology. Most of them occur in immunocompromised and immunosuppressed patients, or in persons with different risk factors, like HIV infection, cancer, transplant of marrow or other transplanted patients, and so on. The fungal superficial infections can cause discomfort and in some conditions can produce disseminated systemic infections. In the conditions of third world developing countries, the lack of industrial medication, and poor sanitation and lack of enough funds for buying modern medicines, the plants can be used as a source of antimicrobial and antifungal medicines. WHO recommends using this important source of medicines and established some guides for this activity.

DISCUSSION
The essential volatile oils
The essential oils are secondary metabolites present in many plants, of course the content of them is tit very variable from species to species, and is influenced by different aspects, like plant parts that are used, vegetation phases or time of the year and of the day, extraction methods and others. Generally, the essential oils contain a mixture of substances and compounds, in very variable amounts, this aspect reduced the possibility to standardize the vegetal origin oils in order to have a scientific control over the therapy.

The essential oils are used on a large scale against different bacteria and pathogenic fungi. An example is the plants Cinnamonum verum, Cymbopogon citratus, C. martini, Syzygium aromaticum used in traditional medicine in India [12]. They contain citral with geraniol and eugenol having inhibitory effects against C. albicans, inhibiting the germ’s tube formation and change the hydrophobicity of cell surface (the antifungal effect was established by macro dilution method). Following analysis, their Minimum Inhibitory Concentration (MIC) was 45-200μg/ml and evident reduction of the infection. The oils with citrate and geraniol reduced the production of proteinase with about 80%. Essential oils from basil (Ocimum sanctum), chamomile (Matricaria camomilla), Oregano (Vaccinium sp.) and thyme (Thymus vulgaris) were also tested on isolates of Candida from clinical samples (C. albicans, C. parapsilosis, C. tropicalis C. glabrata) [19]. The tests were performed according to Kirby Bauer and Vitek methods. Oils of Foeniculum vulgare, Carum carvi and Eucalyptus are well known essential oils with medicinal properties. In a recent study they were tested in vitro on Candida strains, using disk method [21]. As a result of this research, the lowest MIC values at which all the strains were sensible to Carum carvi oils was 0.03mg/ml MIC (C. albicans from laboratory, for example). The tests proved that the essential oils of different medicinal plants can be a serious alternative to chemical antifungals in certain conditions and the concentrations of essential oils play an important role in the treatment. The authors showed that the essential oils extracted from three aromatic plants have a certified antimicrobial effect and at the same time an antifungal potential. They tested extracts (oils) from Foeniculum vulgare (Apiaceae), Carum carvi (Apiaceae) and Eucalyptus sp. (Myrtaceae) in vitro, on C. albicans strains isolated from lung, a laboratory strain and the standard strain ATCC10231, by using disc diffusion and microdilution methods, demonstrating that C. carvi oil has the strongest antifungal activity.

Essential oil extracted from Mentha piperita has a good antifungal activity against Candida yeasts. This is based on the high content of menthol (30 - 50%), carvone and menthone (14 - 32%), as shown by the gas chromatograph analysis. The average MIC against 3 species of Candida (C albicans, C. tropicalis and C. glabrata) was 225 μg/ml, 248 μg/ml and 500μg/ml, respectively [20], results obtained by observing the inhibition areas on agar plates and inhibition of virulence. The toxicity of these compounds is very low. They play a role in inhibition of the transition phase from yeast to hyphal form and release of hydrolytic enzymes. Other species from the Mentha genus (M. longifolia, M. piperita, M. aquatica) contain volatile oils with...
Another classical medicinal plant is Amomum Trifolium (O) and Candida albicans. Another classical medicinal plant is Hypericum perforatum, used as tincture and oil extracts against wounds and dermatological diseases. It contains hypericine and chloromethylchitosan (O) to improve the concentration of xanthenes. By fractionation test, was discovered an ethylacetate fraction containing 6.8% xanthenes, with an MIC of 53.8, 14.18 and 36.52 μg/ml against Candida, Cryptococcus and dermatophytes, respectively [22]. Extensive investigations took place (in the period of 1987-2001) on a large variety of essential oils and extract types from many species of medicinal and aromatic plants [11] and about 500 reports were issued on the antimicrobial and antifungal activities of the extracts and essential oils investigated by agar diffusion methods, dilution methods and factors which are influencing the activity of essential oils. The author focuses on the essential oils from thyme (Thymus vulgaris), oregano (Origanum vulgare), mint (Mentha sp.), cinnamon (Cinnamomum sp), salvia (Salvia sp.) and clove (Trifolium sp) that looks like to have the strongest effect. Origanum essential oils and their effects on Candida strains were investigated, these oils contain phenol derivatives by microdilution method, and the results showed an inhibition of fungal growth at 0.25 mg/ml concentration in vitro. In vivo the daily administration to mice with systemic candidiasis of 8.6 mg Origanum oil with 100 μl olive oil on kg body, resulted in 80% survivability [15]. Eucalyptus oils are intensively used in food products, additives, spices and in pharmaceutical extracts obtained from different species like Eucalyptus sideroxylon and Eucalyptus torquata leaves, stems and flowers [2]. The extracts demonstrated not only antimicrobial activities against some Gram-negative bacteria, like E coli (the others seem to be resistant to the extract), but also against some Gram-positive bacteria. The essential oils have much more antimicrobial and antifungal activity. Regarding the fungi, Aspergillus sp. were resistant to the extracts from plants, but essential oils showed moderate to high inhibitory activity against C albicans, Aspergillus flavus and A. niger. The author showed the Eucalyptus essential oil have cytoxic effects with activity against Human Hepatocarcinoma cell line (HEPG2) and Human breast adenocarcinoma cell lines (MCF7). The essential oils of thyme species are well known folk remedies against all kind of wounds and infections. For example the essential oil from Thymus viciosoi, which contains carvacrol, thymol and p-cymene, is able to produce inhibition of filamentation of C. albicans and has very low MIC 0.04-0.64 μl/ml, the component p-cymene had activity at 2.5-20 μl/ml [23]. The essential oil obtained from seeds of Anethum graveolens [6,7] reduced the ergosterol quantity from cells and attacked the cell membrane of Candida producing damages to their mitochondria.Thymol and their halogenated derivatives 4-chlorothymol, mono-brom-thymol, di-bromo-thymol, iodo-thymol, methylated derivative, have inhibitory effect against Staphylococcus aureus and S. epidermidis (4-chlorothymol is effective at concentrations of about 12.5 ppm-25 ppm and is also effective against Candida albicans) [10]. The same thymol is responsible of inhibition of biofilm formation [4]. The essential oil of Chamaecyparis Lawsoniana [17] obtained from leaves and young stems, contains about 66 compounds, the limonene being the predominant one (77%), but were also identified camphor, p-cymene 7-ol, terpinene 4-ol and others. In vitro test demonstrated that C. albicans is susceptible to this volatile oil with an inhibition area of 20mm. The essential oils obtained from Achillea clavennae L contains (showed by investigation with GC/MS), camphor 29.5%, myrcene 5.5%, 1.8% cineole, 5.3% beta carophyllene 5.1% and linalool 4.9% as main compounds. Susceptibility tests were performed by disk diffusion method, using Watmann paper disks, the results showed antifungal activity, including against Candida albicans [3]. Other example of essential oils with antifungal activity is the allspice oil (Pimenta dioica) evaluated by disk diffusion method on strains of different Candida species (about 75 isolates) isolated from hospital samples [10]. The tests were performed using diluted (3:1, 2:2 and 1:3) and undiluted essential oil and measured for MIC and MFC. Practically this oil inhibited growth of all isolates (24-44mm inhibition area) at MIC 0.9851/ml by micro dilution method. The Juniperus communis extract, which contains monoterpenes, hydrocarbons (78.4%), sabinen (26.2%), alfa pinen (12.9%) and limonene (10.4%), exhibited inhibitory effect against dermatophytic fungi and against Candida species [5]. Other extracts from black pepper (Piper nigrum L.), cardamom (Amomum sp, Elettaria sp), cumin (Cuminum cyminum L.), Boswellia and patchouli (Pogostemon cablin (Blanco) Bent.) were tested for antifungal activity against Candida albicans, C. tropicalis and Trychophyton mentagrophytes (20), alone or together with fluconazole. Practically, the most efficient was the combination of fluconazole with Boswelia essential oil even in 1/10 dilution, against C. tropicalis and at 100 mg/ml, showing a powerful synergic effect.

Essential oils of the same plant can have different concentrations and effects according to their local geographical distribution, fact that was demonstrated. Some natural products can have a synergic antifungal effect administrated together with classical anti fungicides for example, terpenes and fluconazole have an inhibitory effect on Candida biofilms [19]. Ocimum basilicum for example obtained from Togo [14] was used to obtain, by steam extraction from stems and leaves (investigated by GC/MS), five chemotypes (estragol type, linalool/estragole type; methyl-eugenol type; methyl-eugenol/t-anethol type; and anethole type). In vitro activity against fungi showed a MIC of 80-150 μl/ml obtained with the methyl-eugenol type; methyl-eugenol/t-anethole type. Other extract tested for its activity was Pelargonium graveolens essential oil, in which the main compounds were citronellal (24.54%), geranial (15.33%), citronellyl formiat (10.66%) and linalool (9.8%). The oily extract has a good fungicidal activity, at a concentration of 0.25-2.5 mg/ml (8). At the same time, it was demonstrated to have an antioxidant activity, reducing DPPH radicals, an antimalarial effect and produced total inhibition of C. albicans growth. The essential oil of basilicum (Ocimum sanctum L.) contains two main compounds, methyl chavicol and linalool, and has effect on Candida cells induction of apoptosis (lack of nucleus, cytoplasmic shrinkage decrease in cytochrome oxidase activity, externalization of phosphatid serine, DNA fragmentation) [18]. This oil has synergic activity with ketoconazole and fluconazole [1].

**Effects and mechanisms of activity of essential oil components**

The essential oils contain almost 100 different organic compounds classified as terpenes (monoterpens, sesviterpenes), oxygenated compounds (phenols, mono and
sesquiterpenic acids), aldehydes, ketones, esthers, lactones, cumarins, ethers, oxides). The terpenes are compounds with ten atoms, and can be found in many essential oils, with antiseptic, antimicrobial, antifungal and anti-inflammatory properties. According to the same guide, the sesquiterpenes are compounds with 15 carbon atoms, with antimicrobial and antifungal effect as chamazulenes. In the natural products there are oxygenated compounds with antibacterial, antifungal effects, for example thymol, eugenol, and charvacrol. Other antifungal effect substances are the monoterpenes, linalool, citronelol, and terpineols, and sesquiterpenic alcohols (bisabolol). The ketones are also part of the essential oils. Many other components are in low quantities and cannot play a role in treatments.

CONCLUSIONS
The essential oils, as secondary metabolites, can have protective role for the medicinal and aromatic plants against some pests and some fungal and bacterial pathogens, and as well can play a protective effect for the human and animal organisms attacked by such infectious agents.

The oily plants extracts, in fact, as we stated above, contain a large mixture of diverse compounds, in very diverse quantities, making difficult to assess their effects as antifungal and attributing them healing properties. Another thing is their content of possible allergic components. These natural oils cannot be practically standardized, but can be assessed for a minimum content of active substances. In most countries, they are registered and used as supplements or alternative medicine products.

A good decision of medical doctors could be the balance between both. Anyway it is clear that the essential oils could be used as treatment in superficial infections, not in systemic ones, as candidemias or fungal sepsis.

Despite so many studies describing antifungal tests, still their real efficiency in vivo was proved only in a part of the cases. That means that we need more researches to prove their healing effects. Another real problem is the pressure from non-governmental organizations regarding the importance of natural treatments, assigning them too many miraculous properties. That highlights the necessity of additional studies in order to see if the alternative treatments have value for including them in the current medication of fungal infections.

REFERENCES


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