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Anti- mycobacterial effect of plant essential oil and its chemical components

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Abstract

Worldwide, the number of tuberculosis (TB) patients is very high. Increasing number of Mycobacterium tuberculosis organisms are reported to be multi-drug resistant. Even 50 years after the introduction of effective specific chemotherapy against tuberculosis, the number of tuberculosis cases is higher worldwide, and there are an increasing number of cases of infections with organisms resistant to the major anti-tuberculosis agents. Furthermore, side-effects from current medications, increased cost of developing new drugs, the limited commercial potential for drugs for TB and decreasing funds for research from pharmaceutical companies make a negative impact on anti-microbial research. Recently essential oils from plants have been investigated and found to have anti-bacterial and anti-mycobacterial effects. Recent developments in technology have helped in identifying individual chemical constituents in Essential oils. Apart from the essential oil as a whole, these individual chemical constituents also have been found to have anti-mycobacterial effect. Furthermore, few of the individual chemical constituents have been chemically modified to create newer molecules and these newer molecules also have anti-mycobacterial effect. This review emphasizes the importance of continuing research on plant essential oils for newer drug molecules against tuberculosis

Keywords: Essential oil; Mycobacterium tuberculosis; Mycobacteria; Eugenol

Introduction

Natural compounds form the basis for many commonly used medications. For her discovery of the herbal (wormwood plant Artemisia annual) anti-malarial compound the Chinese research scientist Tu Youyou was awarded the Nobel Prize in Physiology or Medicine. In 1972, the compound was purified and named as artemissinin. During the last 20 to 30 years advances in photochemistry and identification of plant components have shown that effective anti-bacterial chemicals are present in plants. Different plant extracts (such as aqueous extracts, ethanol extracts, essential oils) have been reported to have anti-bacterial, anti-fungal, anti-viral, and anti-mycobacterial, anti-oxidant and anti-cancer activities. Researchers are looking into actinomycetes, fungi, cyanobacteria, and plants in their attempt to find newer drug molecules. [1]An essential oil is a volatile (easy evaporation) liquid extracted from plants An essential oil is "essential" in the sense that it contains the "essence of" the plant's fragrance the characteristic fragrance of the plant from which it is derived. Essential oils are generally extracted by distillation, (most frequently by steam or water) EOs are extracted from the leaves, stems, flowers, bark, roots, or other elements of a plant. Angelica, bergamot, lemongrass, mandarin, mint, caraway, celery, citronella, coriander, eucalyptus, geranium, petitgrain, pine, juniper, , lavander, lemon, orange, peppermint, rosemary, sage, Ocimum sanctum and thyme are among the representatives of plants with some of these compounds. Essential oils are often used in aromatherapy [2].

Literature Review

EOs are used in alternative medicine ,in which the healing effects of EOs are ascribed to aromatic compounds in them. EOs and their components are hydrophobic in nature. This property enables the EOs to partition with the lipids in the cell membrane and mitochondria of bacteria leading to disturbance of cell structures. Essential oils may consist of about 20–60 components at quite different concentrations. Essential oils have two or three major components being present at fairly high concentrations and other components are usually present in trace amounts. The components with anti-bacterial activity in EOs are -p-cymene, limonene, menthol, eugenol, anethole, estragole, geraniol, thymol, γ-terpinene, and cinnamyl alcohol [3]. Many researchers have reported that EOs have antibacterial property.We also have reported that the EO from *Ocimum sanctum L.* (Thulasi/Basil) acts against 18 human bacteria. Anti-fungal property of many EOs has been reported by researchers. Anti-viral activities have been reported for essential oil of Pogostemon cablin against influenza virus A (H_2N_2) and the essential oil of Trachyspermum ammi against Japanese encephalitis virus. Essential oils also have anti-inflammatory and wound healing applications. A summary of the experimental evidences of the remarkable wound healing effects of essential oils by in vitro and in vivo tests have been reported. The efficacy of essential oils on human skin ulcers have been evaluated in certain clinical studies. Recently, EOs have been reported to have anti-mycobacterial activity. Table-1 provides the anti-mycobacterial activity of certain EOs from plants.

Author	Plant essential oil	Mycobacterial growth inhibited
El Omaria Khaled et al	*Micromeria barbata*	**Mycobacterium tuberculosis (ATCC® 27294™)**
	Eucalyptus globulus	Multidrug-resistant *M. tuberculosis* (CMUL 157)
	Juniperus excelsa	*Mycobacterium kansasii* (ATCC®12478™) *Mycobacterium gordonae* (ATCC® 14470™).
Mansour Miran et al	*Levisticum officinale*	Multidrug-resistant *Maycobacterium tuberculosis*
Vanessa Pietrowski Baldina et al	*Tetradenia riparia(Hochst.) Codd(Lamiaceae)*	Multi-drug resistant and susceptible *M.tuberculosis* *M.tuberculosis* H37Rv

Rafal Sawicki et al	*Cinnamomumverum* b ark	*M. tuberculosis* H37Ra (ATCC 25177)
Venugopal Jayapal et al	*Ocimum sanctum L*	Multidrug sensitive and resistant *M.tuberculosis* (clinical isolates)
Andrade-Ochoa Sergio et al	*Cuminum cyminum*	H37Rv
	Eugenia caryophyllata	
	Cinnamomum verum	
	Laurus nobilis	
	Pimpinella anisum	

Table 1: Published research articles on the effectiveness of Essential oils against mycobacteria.

Also EOs have been reported to have synergistic anti-mycobacterial activity when combined with anti-tuberculosis drugs in in-vitro studies. Synergistic effects have been documented with *Melaleuca leucodendron* essential oil when combined with kanamycin, isoniazid and rifampicin against *M. tuberculosis* and these combinations increased the potency of isoniazid 4-fold against *M. tuberculosis.* Different plant EOs alone as well as in combination with already approved medication regimens should continue to be investigated as treatment options for TB. Most of these studies on EOs did not provide information on the chemical nature and mechanism of action of the chemical constituents in EO [4]. Therefore, future research should focus on exploring their individual chemical compounds and the molecular mechanisms of actions of essential oils. Among the many chemical constituents of EOs, eugenol has been studied by many investigators for its anti-mycobacterial effect. Eugenol, (4-allyl-1-hydroxy-2-methoxybenzene ;Formula: C10H12O2; Molecular weight: 164.20; CAS number: 97-53-0) a natural substance used as a target molecule for the manufacture of bioactive compounds, was first isolated in 1929 and is extracted from *Ocimum tenuiforum, Cassia fstula, Zieria smithii, and Pimenta racemosa*, *Ocimum sanctum*, etc. It is a phenylpropanoid of the allyl-phenol type, a pale yellow oil with clove odor and spicy taste. Eugenol has numerous applications in the pharmaceutical, food, agricultural, and cosmetics industries. It shows promising anti-bacterial, anti-fungal, anti-viral, anti-inflammatory, anti-oxidant, anti-Leishmanial activities. Eugenol is an antiseptic and used as disinfectant in mouthwash. -Presently zinc oxide eugenol cement has been widely used in dentistry for indirect pulp capping, and as a temporary filling and root canal sealer [5].

Discussion

Researchers have investigated the anti-bacterial and anti-mycobacterial effects of the pure chemical eugenol. Apart from investigating the pure chemical eugenol, recently, investigators have synthesized novel compounds from eugenol and then investigated the anti-bacterial and anti-mycobacterial effects of the novel synthesized compounds in in-vitro experiments. This approach may enhance the biological effects of EO, as well may reduce eventual side effects of EO have carried out the synthesis, purification, characterization, and evaluation of the antioxidant and anti-bacterial potential of 19 eugenol derivatives. The derivatives had a promising anti-bacterial potential against Escherichia coli and Staphylococcus aureus. The triazole ring of eugenol is an important heterocycle in compounds with anti-mycobacterial property. Thiago dos Santos et al had synthesized novel eugenol- derived 1,2,3,-triazole as anti-mycobacterial agents and had reported that four synthesized compounds had anti- mycobacterial activity against rapidly growing mycobacteria. Sachin H.Rohane et al have synthesized some novel hydrozone (which are known to exhibit a wide variety of biological activities, such as anti-bacterial, anti-tubercular, analgesic, anti-inflammatory, anti-viral and anti-fungal) derivatives of eugenol . These newer hydrazine derivatives of eugenol showed anti-Mycobacterium tuberculosis activity against H37Rv by micro plate alamar blue assay method. Aryadne L de Almeida et al have reported that eugenol and three eugenol derivatives (4-allyl-2-methoxyphenyl acetate, 4-allyl-2-methoxyphenyl benzoate, and 4-allyl-2-methoxyphenyl 4-nitrobenzoate) displayed in-vitro activity and synergic effect of eugenol combined with rifampicin, isoniazid, ethambutol, and pyrazinamide againstMycobacterium tuberculosis including multidrug-resistant isolates by resazurin assay. Apart from eugenol certain other chemical constituents of EOs have also been reported to have anti-mycobacterial activity. Rafal Sawicki et al have reported that cinnamaldehyde, the main constituent of Cinnamomumverum bark essential oil had activity against Mycobcterium tuberculosis H37Rv strain. Vanessa Pietrowski Baldin et al have reported that the pure compound 6,7-dehydroroyleanone from the essential oil of the plant Tetradenia riparia showed anti-Mycobacterium tuberculosis effect on clinical isolates (including MDR isolates) of Mycobacterium tuberculosis by Resazurin Microtiter Assay Plate method studied the combinations of anti-tubercular drugs with few main constituents of EO(α-pinene, bisabolol, β-elemene, (R)-limonene, (S)-limonene, myrcene, sabinene), from Mutellina purpurea L., a plant with described antitubercular activity. The combinations of all studied EO constituents with ethambutol or rifampicin resulted in a synergistic interaction against reference M.tuberculosis strains and multi-drug resistant clinical isolates .Nanoparticles (NPs) functionalized with essential oils have been reported to have significant antimicrobial potential against multidrug-resistant pathogens. Nanoparticles may increase chemical stability and solubility, decrease rapid evaporation and minimize degradation of active essential oil components.

Conclusions

In 1998, it was estimated that 60% of the anti-tumor and anti-infective drugs that entered the market or under clinical trial originated from natural products via structural modifications.December 2014 data show that 138 (58.3%) out of 237 anti-infective drugs were products of natural origin or derived from natural products. Therefore, the research on essential oils for anti-mycobacterium molecules has great potential in future. Most of the anti-tuberculosis compounds are being developed by academic institutions or government agencies, which may not have sufficient funds as offered by pharmaceutical companies. Consequently, the fund for research in developing anti-mycobacterial molecules is insufficient. This makes the process of research progression difficult. Therefore, pharmaceutical companies and government organizations should come forward and provide appropriate research funds and encourage the researchers involved in developing new anti-mycobacterial molecules from plants.

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