Biological Activity of Cinnamomum Camphora Essential Oils

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Contributor: Sang-Hwan Lee, Dae-Shin Kim, Seong-Hee Park, Hyun Park

Camphor tree (Cinnamomum camphora) is an ornamental plant that has been cultivated for a long time to obtain wood or camphor. Furthermore, its essential oil can be used as an alternative medicine and is an important source of perfume. Camphor obtained from camphor trees has long been used as a treatment for various symptoms such as inflammation, infection, congestion, muscle pain, and irritation in various regions. Despite many studies focused on the essential oil of the camphor tree, there is a lack of systematic studies of its extraction or separation. Besides, various components of camphor are not fully understood, and further research is needed on the medicinal effects of individual components of C. camphor. The genus Cinnamomum has crucial economic value and theoretical significance.

Keywords: biological activity ; camphor oil ; Cinnamomum camphora

1. Introduction

Camphor tree (*Cinnamomum camphora*) is a member of the Lauraceae family, and is known to be native to India, China, and South Korea, and is now distributed in many other regions such as Australia and the Himalayas [1][2][3][4]. Camphor trees can reach up to several tens of meters (30–40 m) in height and 3 m in diameter and typically grow at 900–2500 m above sea level. The bark is yellow or brown and is vertically split. The leaves alternately have three to several distinct veins, and strong dormant buds surrounded by large, silky-like recesses [5].

This tree is one of the plant species that is highly valued in Asia in terms of its economy and culture, and large-scale cultivation has been established in China and Korea and has been designated and protected as a cultural property [6]. *C. camphora* is designated and protected as a natural monument in Jeju, Korea. KMoCST (Korea Ministry of Cultural Sports and Tourism) announced that it has traditionally been used as a medicinal plant and, in addition to its high biological value, it has high cultural value, providing a glimpse into traditional Asian life [7]. *C. camphora* is facing great pressure and threat, with an increased interest in its value leading to indiscriminate use and a sharp drop in numbers, which could lead to extinction if appropriate protective measures are not taken. To preserve and protect this endangered species, it is crucial to secure genetic diversity data. Maintenance of genetic diversity is essential to the long-term survival of the tree species, without which there may be a risk of its extinction because of a lack of adaptive ability [8]. Camphor trees have many applications in various fields, such as industry, cosmetics, pesticides, pharmaceuticals, timber, ornamental, and many cultural purposes stretching back thousands of years [6]. In the past, various parts of the camphor tree (leaves, stems and fruits) have been used to prepare essential oils and extracts with anti-inflammatory [9], or antifungal [10][11][12] properties, or to treat toothache [13], and spasmodic effects of circulatory and respiratory diseases. Camphor tree is used in the production of perfumes, creams, and balsamic ointments in the cosmetics industry [6][9] and as a treatment for muscle pain, inflammation, and rheumatism in the pharmaceutical sector [14][15][16][17]. The development of modern pharmaceutical technologies provides a theoretical background for the performance of *C. camphora*, which has been used in traditional medicine for a long time. The main research results so far are that the pharmacological effects are mainly derived from essential oils of *C. camphora*. Due to the development of technologies, essential oil can be extracted from various parts of *C. camphora* and components of essential oils exhibiting pharmacological effects can be separated and purified. Essential oils are mainly extracted by distillation.

2. Antimicrobial Activities

The traditional use of *C. camphora* for antiseptic purposes can be attributed to the antimicrobial activity of its essential oil, which has demonstrated a broad range of antimicrobial activities against different pathogens [10][18][19][20]. Poudel et al. [18] reported that the wood EOC showed effective antibacterial activity against *Serratia marcescens*. Likewise, the combined leaf/branch/wood EOC exhibited effective antifungal activity against *Aspergillus niger* and *Aspergillus fumigatus*, and the leaf EOC showed good antifungal activity against *Trichophyton rubrum*, with a minimum inhibitory concentration (MIC) of 78.1 μg/mL.

Chen et al. [19] demonstrated that the essential oil isolated from the leaves of *C. camphora* by hydrodistillation had effective activity against *Staphylococcus aureus* (MICs = 8.0 μg/mL), *Enterococcus faecalis* (MICs = 3.2 μg/mL), *Bacillus subtilis* (MICs = 0.8 μg/mL), *Salmonella enterica gallinarum* (MICs = 1.6 μg/mL), and *Escherichia coli* (MICs = 0.8 μg/mL). Similarly, Bottoni et al. [21] described the essential oil isolated from the aerial parts of the plant as showing discrete inhibitory activity toward the tested bacterial strains *S. aureus*, *E. faecalis*, *Listeria monocytogenes*, and *Pseudomonas aeruginosa* (all MIC equal to 25 mg/mL, except for the MIC against *L. monocytogenes*, which was 12.5 mg/mL). These results are supported in other work in which the leaf EOC demonstrated stronger inhibitory capacity against Gram-negative (*E. coli* and *P. aeruginosa*) than Gram-positive bacteria (*S. aureus* and *B. subtilis*) [6].

Water extracts from *C. camphora* leaves were found to be inhibited in their activity by treatment of 5% for wood fungi *Phanerochaete chryosporium*, *Gloeophyllum traveum*, *Penicillium purprogenum*, *Trichoderma harzianum* and *A. fumigatus* [22]. One wood stain fungus (*Botryodiplodia theobromae*) could also be suppressed when the concentration was increased to 10% [22]. Researchers reasoned that the antimicrobial effect of the water extract could be due to its composition, which included 76.2%, D-camphor and minor constituents, such as 3-methyl-2-butenoic acid (8.6%), 1,8-cineole (4.7%) and 1,6-octadien-3-ol (4.5%).

Wang et al. [23] extracted the EOC from leaves to test its activity against plant pathogenic fungi, such as *Colletotrichum gloeosporioides*, *Botrytis cinerea*, and *Fusarium graminearum*. Notable inhibitory activity was found after 48 h of EOC treatment, with half-maximal inhibitory concentrations (IC_{50}) of 31.74, 35.79, and 38.02 mg/L, for the three separate strains, highlighting the potential use of EOC as a natural preservative for fruits and vegetables. It has been suggested that EOC could be used in the preparation of a strong fungistatic agent against *C. cucurbitarum* infection. Pragadheesh et al. [11] emphasized the inhibitory action of (1*R*)-(+)-camphor against the growth of *Choanephora cucurbitarum*, a wet rot pathogen of *Withania somnifera*. Furthermore, in comparison to (1*R*)-(+)-camphor, *C. camphora* oil revealed superior activity. Fungal growth inhibition by (1*R*)-(+)-camphor and plant essential oil was due to cytoplasm coagulation and hyphal lysis of *C. cucurbitarum.*

Some researchers observed a synergistic antimicrobial effect of constituents of EOC [18][24]. Poudel et al. [18] suggested that the antimicrobial effect of the wood EOC against *S. marcescens* could be due to synergism among the major constituents of the EOC (camphor, 1,8-cineol, α-terpinol, and safrole) and other components. Viljoen et al. showed that a combination of 1,8-cineole and camphor produced a synergistic interaction and improved the antimicrobial effect on *Candida albicans* [24].

3. Anti-Inflammatory Activities

EOCs have long been prescribed in traditional medicine for the treatment of inflammation-related diseases, such as rheumatism, bronchitis and muscle pains. Lee et al. [13] reported that the ethanol extract of *C. camphora* blocked the production of interleukin (IL)-1β, IL-6, and tumor necrosis factor-α (TNF-α) from RAW264.7 cells stimulated by lipopolysaccharide. Another study suggested EOC as a natural treatment for skin inflammation and the possibility of applying medicinal plants to treat various other inflammation-related diseases. Xiao et al. [25] investigated the anti-inflammatory activity of borneol-type EOC in vitro (human erythrocyte membrane stability assay) and in vivo (acute inflame murine model). The essential oil nanoemulsion inhibited heat-induced erythrocyte hemolysis (IC_{50} = 5.29 mg/mL) and hypotonic solution-induced erythrocyte hemolysis (IC_{50} = 0.26 mg/mL). Moreover, both single and repeated topical administration of the EOC on mice auricles reduced xylene-induced auricle swelling. This anti-inflammatory action of *C. camphora* is known to be due to cytokine secretion and control of macrophage-mediated inflammation (IL-1β, IL-6, and TNF-α).

Fu et al. [26] described the amelioration of oxidative stress and inflammation in diet-induced rats treated with *C. camphora* seed kernel oil. This treatment reduced the level of inflammatory markers by increasing the activity of serum glutamate oxaloacetate transaminase and glutamate-pyruvate transaminase and peroxisome proliferator-activated receptor gamma (PPAR-α). Kang et al. [27] described the efficacy of EOC from leaves in treating allergic inflammation, such as atopic dermatitis. The extract demonstrated a notable anti-inflammatory effect in human adult low-calcium high-temperature keratinocytes, and ameliorative effects on 2,4-dinitrochlorobenzene-induced atopic dermatitis in mice. These findings will facilitate the development of EOC as a new and natural therapeutic agent for inflammatory skin conditions.

4. Insecticidal and Acaricidal Activities

Essential oil-based pesticides have a wide range of pest management applications with several advantages, such as being readily available, renewable, and readily degraded to minimize environmental side effects [10]. Currently, there is increasing use of plant-derived essential oils as insecticides and repellents in agriculture and the health sector.

The EOC has been found to have a certain degree of mosquito repellence. Xu et al. [28] confirmed the potent larvicidal efficacy of EOC against the mosquito *Anopheles stephensi*. Satyal et al. [10] examined the insecticidal activity of leaf EOC against mosquito (*Culex pipiens*) and midge (*Chaoborus plumicornis*) larvae, cabbage white butterfly (*Pieris rapae*) larvae, termites (*Reticulitermes virginicus*), fruit flies (*Drosophila melanogaster*), and red imported fire ants (*Solenopsis invicta* × *richteri*). The oil showed mosquito and midge larvicidal activities but was most effective against cabbage butterfly larvae, fruit flies, and fire ants (median lethal concentration (LC_{50}) = 186, 153, and 176 μg/mL, respectively).

Chen and Dai [29] reported that the ethanol extract of *C. camphora* displayed remarkable acaricidal activity against the mite *Tetranychus cinnabarinus*. The most active constituents of the extract were 2,4-di-*tert*-butylphenol and ethyloleate, with LC_{50} values of 1850.94 and 2481.65 mg/kg, respectively, after a seven-day treatment in a potted seedling experiment.

Jiang et al. [30] reported the insecticidal potential of seed, leaf, and twig EOC against cotton aphids. The seed EOC exhibited the highest repellent activity (89.86%, after 24 h of treatment at a concentration of 20 μL/mL). The LC_{50} values of 245.79, 274.99, and 146.78 mg/L were reported for the three essential oils after 48 h of treatment, respectively. Linalool was a major contributor to the insecticidal and repellent effects [31].

5. Antioxidative Activities

As alluded to above, *C. camphora* seed kernel oil increased the antioxidative activity and lowered the concentration of malondialdehyde (a biomarker of lipid peroxidation and oxidative stress) in diet-induced rats by increasing the concentration of superoxide dismutase and catalase [26]. Liu et al. [32] demonstrated the in vitro antioxidative property of the flavonoids extracted from *C. camphora* leaves. The flavonoids exhibited a dose-dependent increase in the antioxidant activity, as measured by the 1,1-diphenyl-2-picryl-hydrazyl (DPPH) free radical scavenging assay and the ferric reducing antioxidant power assay, with remarkable results compared to commercial antioxidants. Similar findings were reported by Lee et al. [13]. Most of the antioxidative/free radical scavenging effect was observed in the butanol extract (in the DPPH assay) and the ethanol extract (in the xanthine oxidase activity assay) of *C. camphora*, with IC_{50} values of 14 and 15 μg/mL, respectively.

6. Allelopathic and Algicidal Activities

Allelochemicals from plants are considered effective, economic, and environmentally friendly herbicides and algaecides due to their effective inhibitory action against herbs and algae, convenient preparation, and easy degradation in nature. Satyal et al. [9] evaluated the allelopathic activities of Nepalese *Cinnamomum* essential oils in terms of inhibition of seed germination, as well as inhibition of seedling growth against a representative dicot (lettuce, *Lactuca sativa*) and a representative monocot (perennial ryegrass, *Lolium perenne*). *Lactuca sativa* seed germination was notably inhibited by EOC (IC_{50} = 149 μg/mL), as well as its major component, camphor (IC_{50} = 239 μg/mL). Furthermore, the EOC inhibited the seedling growth of *L. perenne* and *L. sativa*, with relatively greater efficacy against *L. sativa.*

A number of studies have shown the potential value of *C. camphora* as an algaecide. Yakefu et al. [33] observed the inhibitory effects of the water and methanol extracts, respectively, of fresh *C. camphora* leaves on *Microcystis aeruginosa* and *Chlamydomonas reinhardtii* algae cell growth by inducing chlorophyll degradation and reducing photosynthesis. Methanol extracts showed superior inhibitory effects to water extracts at the same concentration because of a greater number and higher concentration of compounds in the methanol extracts. It was thought that linalool and camphor were the major compounds responsible for the observed anti-algal activity. However, other terpenoids in the *C. camphora* extracts might also contribute to the inhibitory effects. In other studies, cell growth of the algae *Chlorella vulgaris* and *C. reinhardtii* was reduced when exposed to 1,8-cineole and limonene due to the degradation of photosynthetic pigments and decreased photosystem II efficiency [33].

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