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The bioactivity of essential oils and their flavor and fragrance components have been known since ancient times. Essential oils are a mixture of numerous compounds characterized by an essence of aromatic plants. Currently, approximately 3000 essential oils are known, 300 of which are commercially important, in particular for the pharmaceutical, food, household and cosmetic industries. Essential oils have been known to have various bioactivities including antibacterial, antiviral, anti-inflammatory, antifungal, antimutagenic, anticarcinogenic, and antioxidant as well as other miscellaneous activities. Consequently, studies on the biological activities of essential oils have become increasingly important in the search for natural and safe alternative medicines in recent years. This review discusses various biological activities of essential oils and their components that have been reported in scientific references.

Keywords: Antibacteria; antioxidant; aromatherapy; biological activities; essential oil; volatile compounds

Introduction

Essential oils are present in various aromatic plants generally grown in tropical and subtropical countries. They are obtained from various parts of the aromatic plants, including leaves, flowers, fruits, seeds, buds, rhizomes, roots, and barks. Several techniques have been used to obtain essential oils from the plant. They are hydrodistillation, solvent extraction, cold pressing, and supercritical fluid extraction (1–3). Among these techniques, essential oils are most commonly obtained by a steam distillation method developed in the Middle Ages in the Middle East.

There is a record that Hippocrates, an ancient Greek physician, referred to aromatic plants as the ‘father of medicine’. Aromatic plants, which contain essential oil, have been used since ancient times for various purposes including medical treatments, food preservatives, and flavoring food. The term ‘essential oil’ was used for the first time in the sixteenth century by Paracelsus von Hohenheim, who named the effective component of a drug, in his book, ‘Quinta essential’ (4). In ancient Egypt, essential oils obtained from aromatic plants were used for disease prevention and treatment. Later, the Greeks and Romans inherited Egyptian practices of using essential oils in aromatherapy and expanded them to improve their life quality. For example, they used baths infused with the oils of jasmine, lavender, or ylang-ylang to stimulate mental relaxation.

Nowadays, approximately 3000 essential oils are known, about 300 of which are commercially available. The major constituents of essential oils are terpenes/terpenoids and aromatic and aliphatic compounds, which are characterized as low-molecular-weight aroma chemicals (5–8). Generally, essential oils are comprised of two or three major components in relatively high concentrations (20–95%) and other components present in trace levels. Components with relatively high concentrations in essential oils are *d*-limonene (over 80%) in *Citrus* peel oils, carvacrol (30%) and thymol (27%) in *Origanum compactum* oil, α-/β-thujone (57%) and camphor (24%) in *Artemisia herba-alba* oil, 1,8-cineole (50%) in *Cinnamomum camphora* oil, α-phellandrene (36%) and limonene (31%) in *Anethum graveolens* leaf oil, carvone (58%) and *d*-limonene (37%) in *Anethum graveolens* seed oil, and menthol (59%) and menthone (19%) in *Mentha piperita* oil. Generally, these major components of essential oils determine their biological properties, details of which are described in two comprehensive reviews on the biological activities of essential oils (9,10).

In the modern era, essential oils and some of their components have been used in various products such as cosmetics, household cleaning products and air fresheners, hygiene products, agriculture, and food, as well as in medicinal uses. Essential oils are also used in aromatherapy and other para-medicinal practices (11–13). Since organic chemistry developed to provide synthetic medicines in the middle of the twentieth century, the use of essential oils for medicinal treatment diminished compared with their use in cosmetics and foods. However, the demand for safe and natural alternative medicines has risen as a consequence of

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consumers' concern about the toxicity of synthetic chemicals (14, 15). Therefore, essential oils have recently begun to receive much attention as possible sources of safe and natural alternative medicines once again because they have been known to possess various medicinal activities, including antioxidant (16, 17), anti-inflammatory (18, 19), antimicrobial (20, 21), antiviral (22, 23), and anticarcinogenic (24). Consequently, studies on essential oils to evaluate the pharmacological properties in order to find possible alternative medicines have become active in recent years.

This review discusses the various biological activities of essential oils and their components, which have been reported in scientific references. Figure 1 shows the structure of the chemicals discussed in this review with respect to their biological activity.

Antioxidant activity

Antioxidant activity is one of the most intensively studied subjects in essential oil research because oxidation damages various biological substances and subsequently causes many diseases, including cancer (25, 26), liver disease (27), Alzheimer's disease (28), aging (29), arthritis (30), inflammation (31), diabetes (32), Parkinson's disease (33, 34), atherosclerosis (35), and AIDS (36). As a result, many diseases have been treated with antioxidants to prevent oxidative damage (37).

Recently, many researchers have been investigating the antioxidant activity of different essential oils in order to search for safe natural antioxidants. Consequently, various studies have shown that essential oils are ideal natural sources of antioxidants. Thyme essential oil exhibited the greatest antioxidant effect among 25 essential oils tested in one study, followed by clove leaf, cinnamon leaf, basil, eucalyptus, and chamomile (38). The essential oils of coriander, eucalyptus, juniper, cumin, basil, cinnamon, clove, and thyme also possessed appreciable antioxidant activity (1, 39, 40). The essential oil of Egyptian corn silk showed potent antioxidant activity, which was attributed to the high content of thymol (20.5%) and carvacrol (58.1%) (41). *Thymus spathulifolius* essential oil also possessed antioxidant activity because of the high content of thymol (36.5%) and carvacrol (29.8%) (42).

There have also been reports on the *in vivo* antioxidant activity of essential oils. Dietary supplementation of oregano oil to rabbits delayed lipid oxidation (43). When the same oil was fed to turkeys, the reduction of lipid oxidation effect, which was comparable with that of α-tocopheryl acetate, was observed (44). The essential oils of *Salvia cryptantha* and *Salvia multicaulis* had higher antioxidant activity than those of ascorbic acid or BHT (45). The essential oil of *Achillea millefolium* subsp. *millefolium* (Asteraceae) exhibited a hydroxyl radical scavenging effect by inhibiting the non-enzymatic

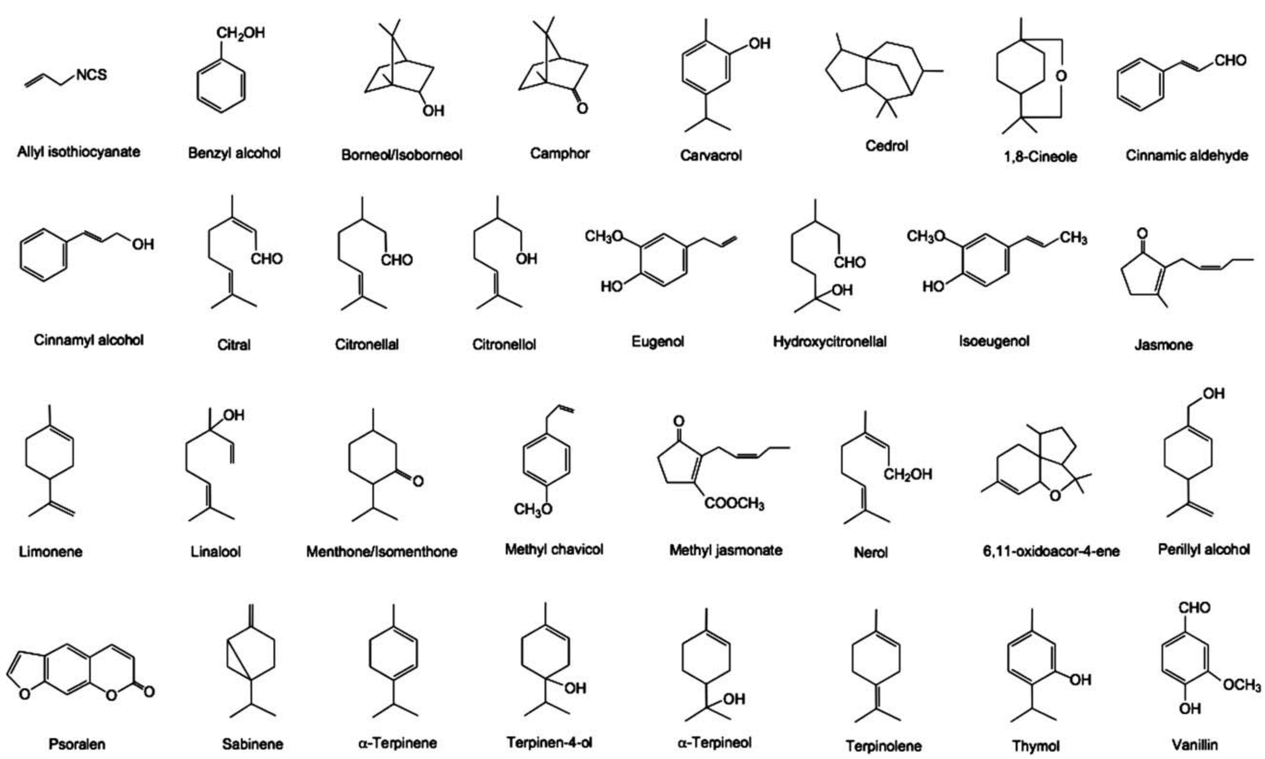

Figure 1. The structure of the chemicals discussed in this review with respect to their biological activity in alphabetical order.

lipid peroxidation of rat liver homogenate (46). In addition, *Curcuma zedoaria* essential oil was found to be an excellent radical scavenger (47).

Many aroma components of essential oils, such as terpenes and terpenoids, were proposed to contribute to the antioxidant activity of essential oils (38); including α-terpinene, β-terpinene, and β-terpinolene in tea tree (*Melaleuca alternifolia*); 1,8-cineole in *Mentha aquatica* L., *Mentha longifolia* L., and *M. piperita* L.; menthone and isomenthone in *M. longifolia* and *M. piperita*; thymol, eugenol, and linalool in black cumin, cinnamon bark, and ginger (48); and thymol and eugenol in thyme and clove leaf (38). Essential oils of *Thymus caespititius*, *Thymus camphorates*, and *Thymus mastichina*, which showed comparable antioxidant activity to that of α-tocopherol, contained high levels of linalool and 1,8-cineole. The essential oil of lemon balm (*Melissa officinalis* L.) containing neral/geranial (citral), citronellal, isomenthone, and menthone showed strong antioxidant activity (49).

These reports suggest that essential oils are rich sources of natural antioxidants and can be used to replace synthetic antioxidants to prevent various degenerative diseases (50).

Antibacterial activity

Many synthetic antibacterial chemicals have been used as preservatives in foods to control natural spoilage and to prevent/control the growth of pathogenic microorganisms. Since consumers' concern has come to focus on the toxicity of synthetic chemicals, antibacterial compounds found in natural plants have begun to receive much attention as safe food additives. Various natural plants are known to have antibacterial activity. For example, spices and herbs have been used as a preservative to control pathogens in foods for many years. However, only a few essential oils, such as *Nandina domestica* Thunb, are known to be useful as a potential alternative to synthetic preservatives (51).

Many studies showed that essential oils had antibacterial properties against a wide range of bacterial strains, such as *Listeria monocytogenes, Listeria innocua, Salmonella typhimurium, Escherichia coli, Shigella dysenteria, Bacillus cereus, Staphylococcus aureus*, and *S. typhimurium* (52). Some essential oils demonstrate antibacterial activity against zoonotic enteropathogens including *Salmonella* spp. *E. coli* O157, *Campylobacter jejunii*, and *Clostridium perfringens*. Mixtures of different essential oils such as oregano and thyme, oregano and marjoram, and thyme and sage exhibited strong antibacterial effects against *B. cereus*, *Pseudomonas aeruginosa*, *E. coli* O157:H7, and *L. monocytogenes* (53). The essential oil of oregano was effective against *P. aeruginosa* and *E. coli* (54). Another report indicated that thirty out of sixty essential oils exhibited strong inhibitory activity against *Helicobactor pylori*, which is associated with severe gastritis and an increased incidence of peptic ulcers (55). Generally, essential oils in decreasing order of antimicrobial activities are reportedly: oregano > clove > coriander > cinnamon > thyme > mint > rosemary > mustard > cilantro/sage (56).

Among the individual constituents of essential oils, carvacrol, isoeugenol, nerol, citral, and sabinene exhibited potent anti-*H. pylori* effects (57).The major components of thyme and oregano essential oils, thymol and carvacrol, inhibited pathogenic bacterial strains, such as *E. coli*, *Salmonella enteritidis*, *Salmonella choleraesuis* and *S. typhimurium* (56). Eugenol, terpenen-4-ol, and carvacrol showed an inhibitory effect against the growth of four strains of *E. coli* O157:H7 and *L. monocytogenes* (58).

Antiviral activity

Synthetic antiviral drugs have been used for the curing of Herpes simplex virus (HSV; type 1, 2), which causes some of the most common viral infections in humans. These viral diseases have been treated by some essential oils. The essential oil of *M. officinalis* L., which contains citral and citronellal, inhibited the replication of HSV-2 (59). Of these, lemongrass essential oil possessed the most potent anti-HSV-1 activity and completely inhibited viral replication after incubation for 24 hours, even at a concentration of 0.1%. The essential oils of eucalyptus, *Santolina insularis*, and Australian tea tree also showed the antiviral effects against HSV-1. Isoborneol, a common monoterpene alcohol, showed dual virucidal activity against HSV-1 and specifically inhibited the glycosylation of viral polypeptides (60). Junin virus was inhibited by the essential oil of *Lippia junelliana* and *Lippia turbinate* (61). An appreciable number of essential oils have reportedly shown potent antiviral activity but there is, unfortunately, virtually no study into the antiviral activity of essential oils against the major viruses of our era, such as HIV and hepatitis C (62).

Anti-inflammatory activity

Inflammation has been known to be associated with certain diseases including hypertension, cancer, and stroke (63). The traditional use of essential oils as anti-inflammatory agents suggests that they possess potent anti-inflammatory activity. Aloe vera is one of the best-known plants with anti-inflammatory activity (64). The aloe vera essential oil produced by cold press is a pale/translucent oil and used as a carrier oil in aromatherapy. Enhancement of wound healing by use of aloe vera was observed in diabetic rats (65) and in various cases of dermal ischemia (66). Even though there are many reports on the anti-inflammatory activities of aloe vera, studies on the activity of its essential oil are limited (67, 68). Aloe vera extract demonstrated anti-inflammatory activity toward carrageenan-induced edema in the rat paw and inhibition of cyclooxygenase activity (18). Aloe vera essential oil exhibited the greatest lipoxygenase inhibitory activity (96%), followed by thyme oil (86%) and bergamot oil (85%) at a concentration of 0.5 μg/mL. Chamomile oil showed slight lipoxygenase inhibitory activity at 0.5 μg/mL but showed strong lipoxygenase inducing activity at 5 μg/mL (−123%) (38). The essential oil of licorice root also exhibited strong anti-inflammatory activity in a lipoxygenenase inhibitor screening anti-inflammatory assay (69).

Antifungal activity

Some essential oils have demonstrated a broad range of natural fungicidal effects against post-harvest pathogens. The antifungal activities of essential oils could be applied in the vapor phase for food storage (70). However, more study is required for vapor-phase application because possible deterioration of the food material could still occur (71). Carvacrol and thymol were reported to be effective against food-borne fungi, including *Aspergillus niger*, *Aspergillus flavus,* and *Aspergillus parasiticus* (72). Thymol, cinnamic aldehyde, and eugenol extracted from clove and cinnamon oils also showed antifungal properties (73). Water-distilled essential oil from the leaves and flowers of *Micromeria nubigena* H. B.K. (Lamiaceae) exhibited antifungal activity (74). *Aspergillus parasiticus* growth and aflatoxin production have been inhibited by the essential oils of *Thymus vulgari* and *Citrus aurantifolia*, whereas *Mentha spicata* L., *Foeniculum miller*, and *Artemisia dracunculus* inhibited fungal growth only. *Carum carvi* L. controlled aflatoxin production without effect on fungal growth (72). Linalool, methyl chavicol, and vanillin extracted from sweet basil and vanilla also exhibited the same inhibitory effect on aflatoxin production (73).

Essential oils of *Eugenia chlorophylla* O. Berg. (Myrtaceae) and thyme showed activity against molds and yeasts (73, 75, 76). Oleoresin extracted from cinnamon and clove oils inhibited mycotoxin-producing *Aspergillus* and *Penicillium* species (73). Less volatile phenolic compounds, such as allyl isothiocyanate and citralon, in mustard and lemongrass oils, were much more effective than volatiles such as terpene hydrocarbons (77). However, essential oils containing high levels of terpene hydrocarbons, such as marjoram oil, exhibited appreciable antifungal activity (78).

Antimutagenic activity

Mutations can be prevented in various ways, including inhibiting the penetration of mutagens into cells, adding antioxidants, which inactivate the free radicals produced by mutagens, activating cell antioxidant enzymes, and detoxificating mutagens by activating enzymes with plant extracts (79,80). Antimutagenic compounds are effective by promoting error-free DNA repair or by inhibiting error-prone DNA repair (81). There has been no investigation on the type of antimutagenicity involving DNA repair by terpenic and phenolic compounds from essential oils since the work by Kada and Shimoi on *E. coli* (81). The chemical compounds extracted from aromatic plants, such as α-terpinene, α-terpineol, 1,8-cineole, *d*-limonene, camphor, citronellal, and citral modulated hepatic mono-oxygenase activity by interacting with promutagen or procarcinogen xenobiotic biotransformation (82). It has been demonstrated that mitochondrial damage and apoptosis/necrosis in the yeast *Saccharomyces cerevisiae* were reduced by essential oils (62). Recent studies shown that certain essential oils exhibited antimutagenicity toward mutation caused by UV lights (10, 83).

Anticarcinogenic activity

Non-nutrient compounds in the diet, including monoterpenes, inhibited experimental carcinogenesis. Several experimental and population-based studies indicated that isoprenoids in the diet play an important role in the reduction of cancer incidence (84–86). Limonene, a major component in many *Citrus* essential oils, exhibited chemo-preventive and therapeutic effects against mammary tumors in rats and metastasis of human gastric cancer. The essential oil of *Citrus limon* modulated the apoptosis through the activation of the interleukin-1β-converting enzyme-like caspases. *d*-Limonene and perillyl alcohol and their active serum metabolites inhibited protein isoprenylation (87).

Miscellaneous activities

Digestive activity

Certain aromatic plants have been used for patients with digestive problems (88). Some studies suggest that essential oils and their components have digestive activity (89). For example, lavender essential oil is reported to affect the gastrointestinal function through activation of the vagus nerve (90). The olfactory stimulation generated by lavender oil scent and its main component linalool activates gastric nerves that enhance food intake by rodents, while grapefruit oil fragrance and its main component *d*-limonene show the opposite effect (91).

Photo toxicity

Some essential oils are known to contain photoactive compounds. Psoralens present in an essential oil of

Citrus bergamia form mono- and bi-adducts under UV light, and subsequently lead to mutagenicity and cytotoxicity (92). It has been noted that *Fusanus spicatus* wood essential oil was not phototoxic but highly cytotoxic, suggesting that cytotoxicity is rather antagonistic to phototoxicity. In the case of phototoxicity, essential oils penetrate into the cells without damaging the membranes. Cytotoxicity or phototoxicity was proposed to be dependent on the type of chemicals present in the essential oils and the producing different types of radicals with or without light exposure (62).

Other activities

There have been reports on the activities of essential oils and their components in addition to the ones described above, including inhibiting resorption in experimental rats by monoterpenes (93), antiosteoporotic activity by (2*E*,6*R*)-8-hydroxy-2,6-dimethyl-2-octenoic acid from *Cistanche salsa* oil (94), preventing bone loss in an osteoporosis patient by pine essential oils and monoterpenes such as borneol, thymol, and camphor (93), and modulating the neuronal responses related to nociception, pain and anxiety by lemon oil (95, 96).

Potential activity toward slowing the progress of Alzheimer's disease was demonstrated in a pilot open-label study involving oral administration of the essential oil of *Salvia lavandulaefolia* Vahl. (13). Chinese angelica (*Angelica sinensis*), which is the most important female tonic remedy in Chinese medicine, exhibited an anxiolytic-like effect (97). Aloe vera leaf gel extract had a protective effect comparable with glibenclamide against hepatotoxicity produced by diabetes (98).

Proposed mechanisms of bioactivity

The activity of plant-origin antimicrobials may depend on factors such as the method of extraction, growth phase of cultivation, culture medium used for testing, and contents of various components including fat, protein, water, and surfactants in addition to the aroma chemicals (99, 100). It is indicated that there is an optimum range of hydrophobicity involved in the activity level of essential oils (101). For example, the vapor phase application of mustard and clove essential oils showed clear differences in amount of activity observed compared with the same oils produced by direct contact method (102). The antimicrobial activity of a combination of cinnamon and clove essential oils showed higher activity in the vapor phase than in the liquid phase (102). In another study, when the oxygen level was decreased, the sensitivity of microorganisms to the essential oils increased (56). Application of nisin with carvacrol or thymol was effective against *B. cereus* with temperatures increasing from 8°C to 30°C (56). Oregano essential oils have increased the shelf life of fresh chicken in combination with modified atmospheric packaging (103).

Synergism occurs when the combined effect of substances is higher than the sum of the individual effects. Antagonism happens when a combination shows less effect compared with the individual applications (56). Some synergistic effects of essential oil components have been reported in previous studies (87, 104), including carvacrol and thymol against pathogenic microorganisms (105), rosemary extract and nisin toward bacteriostatic and bactericidal activity (106), linalool and 1,8-cineole toward *E. coli* (107), and cinnamaldehyde and eugenol against *Staphylococcus* sp., *Micrococcus* sp., *Bacillus* sp. and *Enterobacter* sp. (56). In addition, thymol and carvacrol, found in cilantro, coriander, dill, and eucalyptus essential oils, showed synergistic and antagonistic effects with combinations of different proportions. When clove and tea tree essential oils were used to protect against *E. coli* O157:H7, off-flavors were minimized in addition to the synergistic effect (108).

Synergism and antagonism phenomena are important in evaluating the biological activities of essential oils because over 1000 components are present in essential oils either as high concentration major components or as minor trace components. For example, typical major components in some essential oils are α-pinene (44.2%), thymol methyl ether (22.2%), and camphor (10.2%) in juniper berry (*Juniperus drupacea* L.) essential oil; benzyl alcohol (20.4%), furfural (7.4%), ethanol methyl pentyl acetal (5.9%), and thymol (5.1%) in caper bud (*Capparis ovata* desf. var. *caescens*) oil (40).

The mechanisms of antibacterial activity of essential oils are not yet completely understood (14, 56, 109–111). Therefore, more investigations of essential oils to maximize their use as pharmacological products are in order (56, 72, 108, 112, 113).

Use and method for aromatherapy

Inhalation

Inhalation of essential oils or their volatile components plays a significant role in controlling the central nervous system. For instance, aroma inhalation of *Storax pill* essential oil and preinhalation of *Acorus gramineus* rhizome essential oil are used in Chinese folk medicine for the treatment of epilepsy (114, 115). These oils showed an inhibitory effect toward the central nervous system via the gamma-aminobutyric acid (GABA)-ergic neuromodulation system. This effect originates from the enhancement of GABA levels in the brain (115). The fragrance compounds, *cis*-jasmone and methyl jasmonate, which characterize the aroma of *Jasminum randiflorum,* have a tranquilizing effect on the brain upon inhalation (116). They significantly increased the sleeping time of mice induced by pentobarbital, suggesting that these fragrant compounds were absorbed by the brain and subsequently potentiated the GABA receptor response. Cedrol, which is a major component of cedar wood essential oil, showed a sedative effect and prolonged pentobarbital-induced sleeping time in rats upon inhalation (117). The vapor of lavender essential oil or one of its main components, linalool was used for the treatment of menopausal disorders via inhalation (118). Lavender (*Lavandula hybrida* Reverchon 'Grosso') essential oil demonstrated analgesic activity when inhaled (119).

Inhalation of peppermint essential oil vapor has been used for patients with disseminated and infiltrative pulmonary tuberculosis (120). The vapor phase cinnamon and clove oils also inhibited Gram-positive and Gram-negative pathogenic bacteria (121). Inhaling the vapor of pepper oil induced a 1.7-fold increase in plasma adrenaline concentration, whereas inhaling the vapor of rose oil caused a 30% decrease in adrenaline concentration (122). The plasma adrenocorticotrophic hormone levels increased by stress in rats were significantly reduced by inhalation of chamomile essential oil. The same effect was achieved by the intraperitoneal injection of a synthetic tranquillizer, diazepam (118). Inhalation of the volatiles of lavender and monarda essential oils reduced the cholesterol content in the aorta and also reduced atherosclerotic plaques but had no effect on the blood cholesterol level (123).

Massage

Inflammatory diseases, such as allergy, rheumatism, and arthritis, are often treated by massage therapy with an essential oil (124, 125). Various effects of the topical application of essential oils have been reported including suppressing allergic symptoms by tea tree oil (126, 127) and lavender oil (128) as well as by their volatile constituent, terpenen-4-ol (129), suppressing the inflammatory symptoms by a geranium essential oil (124), and alleviating fatigue in cancer patients by a lavender essential oil (130). A cleansing gel fragranced with lavender oil had a transient effect of improving mood and making people feel more relaxed (131).

The cutaneous treatment with an essential oil of *M. officinalis* (lemon balm) was effective toward patients with severe dementia – associated with brain diseases, including Alzheimer's, stroke, and other rarer conditions (132). On the other hand, inhalation of lavender essential oil was not effective in severely demented patients (133). Cutaneous application of the essential oil through massage may therefore be necessary to achieve the effect on patients with dementia.

It should be noted that some essential oils are potentially toxic (134, 135). Various allergic reactions were observed when applied to the skin via massage (136–140). These allergic reactions may be caused by certain constituents, such as benzyl alcohol, cinnamyl alcohol, eugenol, isoeugenol, and hydroxycitronellal (141). Therefore, essential oils containing these components should be handled carefully to avoid any adverse effects (142).

Conclusion

Chemicals derived from natural plants such as essential oils should be considered potential alternative medicines because consumer concerns today have come to focus on the general toxicity of synthetic chemicals. Essential oils have shown to have beneficial medicinal activities including antibacterial, antiviral, anticarcinogenic, and antioxidant effects. However, it is important to develop a better understanding of the biological activities of essential oils for use in the prevention of various degenerative diseases without relying on synthetic chemicals. Activity of essential oils against the major viruses of twenty-first century such as HIV and hepatitis C should be studied more intensively. Moreover, essential oils should receive much more attention as natural and safe medicines compared with synthetic ones as a means to save and protect the ecological equilibrium.

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