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Review Article

Biological, Functional and Network Pharmacological Exploration of Essential Oils in Treatment and Healthcare of Human Diseases

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Abstract

Essential oils (EOs) are natural products with bioactive functions that are obtained from various plant species, including *Lavandula angustifolia* and plant parts, through extraction methods, such as hydro-distillation, steam distillation and cold pressing, which can be dated back to ancient Egyptian and Greek times. Although various EOs are effective for disease treatment, such as human infectious diseases and mental disorders, the specific pharmacological mechanisms remain unclear due to its complex composition. Previous studies have attempted to recruit pharmaceutical analysis techniques, such as HPLC and MALDI-TOF, in order to elucidate the compositions of EOs. However, these have provided limited information on the mechanism of the bioactive functions of EOs. In recent years, network pharmacology has emerged as a convenient and appropriate approach to study the molecular mechanism of traditional medicines. To date, there is a lack of updated reviews on the recent progress of network pharmacology in the field of interactions between EOs and human diseases. Therefore, the present study scrutinized recent and important literatures in the field of network pharmacology and EOs, aiming to provide a timely yet brief overview of EOs as a potential treatment for diseases via network pharmacology, and facilitating the application of EOs as a complementary medicine and therapy for human diseases.

Introduction

Essential oils (EOs), which are also known as volatile oils, are volatile aromatic compounds extracted from flowers, leaves, seeds, roots and other parts of plants,[1] which are biologically active natural products. The composition of EOs usually contain terpenes, aldehydes, esters, alcohols, polyphenols and other compounds.[1–3]

Keywords: Essential oils; Network pharmacology; Infectious disease; Chronic Disease; Mental disorder.

Abbreviations: AD, alzheimer's disease; EOs, essential oils; GO, gene ontology; HS, herba siegesbeckiae; KEGG, kyoto encyclopedia of genes and genomes; RA, rheumatoid arthritis.

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Common EOs originate from medicinal plants in traditional medicine and aromatic plants in nature, such as lavender, lemon, tea tree, rose, orange, frankincense, myrrh and mint. EOs are usually added to various skin care products and ointments, and are widely used in perfumes and aromatherapy.[4,5] Furthermore, various studies have reported that EOs have good effects in relieving stress,[5] improving mental disorders,[6] anti-viral infection,[7] anti-inflammation,[8] bacterial sterilization,[9] anti-diabetes,[10] anticancer,[11] and so on. However, the mechanism of action of EOs in the treatment of these diseases has not been fully elucidated, because EOs have complex compositions, and there may be synergistic or antagonistic effects among these components.[7] Therefore, it remains difficult to fully dissect the mechanisms of EOs in the treatment or remission of a variety of human diseases using traditional techniques and methodologies.

Network pharmacology investigates the functions of multi-component drugs in an overall perspective, which systematically and comprehensively sheds light on the mechanism of the drug treatment of a particular disease.[12] Therefore, network pharmacology has been widely applied in the field of traditional Chinese

Fig. 1. Schematic illustration of the applications of essential oils in human diseases.

medicine,[13] such as the research and development of new drugs, and the exploration of recipe mechanisms.[14–16] In terms of the pharmacological functions of EOs, network pharmacology can provide novel insights and strategies for the in-depth understanding of EOs and its mechanism in treating or alleviating diseases, providing theoretical results for further experimental verifications. The present mini-review focused on the components and functions of EOs, the application of EOs for the alternative or adjuvant treatment of human diseases, and the exploration of EOs in the treatment of human diseases and its mechanisms via network pharmacology, in order to provide reference for further EO studies.

Applications of EOs in the treatment of human diseases

EOs are a class of complex plant secondary metabolites,[1] which contain a variety of bioactive components. Different components in EOs have versatile functions in plants, such as defense against various predators and the inhibition of infection of pathogenic microorganisms.[1] These components have the characteristics of small molecular weight, strong penetration, and easy absorption by the human body.[3] Furthermore, these have important and effective roles in anti-infection, the alleviation of chronic diseases, and the improvement of poor mental disorders, and have a wide range of application prospects in the pharmaceutical industry for drug discovery, design and development. The schematic illustration of the applications of EOs in human diseases is shown in Figure 1.

Anti-infection effects of EOs

Infectious diseases are usually caused by microbes, such as viruses, bacteria, fungi and nematodes. It has been reported that EOs exhibit the properties of significantly inhibiting various microbial pathogens. For example, *Origanum vulgare* (Oregano) EO has good inhibitory effects on common pathogens and fungi, such as *Candida albicans, Staphylococcus aureus*, *Escherichia coli* and *Salmonella*, based on the broth microdilution method.[9] Furthermore, the results of *in vivo* and *in vitro* studies have revealed that EOs, such as *Artemisia annua*,[17] *Vernonia polyanthes* Less (Asteraceae),[18] *Chenopodium ambrosioides*[19] and *Piper Species*,[20] can kill Leishmania, which is a single-celled parasitic organism that belongs to the genus trypanosomes, and is responsible for the disease, leishmaniasis. In addition, the EOs of *Piper Species*[20] and *Eucalyptus*[21] can inhibit the growth and reproduction of tuberculosis-causing bacteria in *in vitro* antibacterial experiments. Moreover, *Eucalyptus* EO has antiviral activity,[7] and *peppermint* EO has been shown to inhibit herpes simplex virus *in vitro*.[22] The above-mentioned evidence confirms that EOs have potential clinical values in the prevention, control and treatment of infectious diseases.

In addition, *in silico* investigation has been adopted to explore

the potential functions of EO components in the treatment of emerging infectious diseases. A total of 171 EO components were selected for the computer-aided molecular docking analysis,[23] and the compound with the highest docking score with SARS-CoV-2 M^{pro} was sesquiterpene hydrocarbon (*E*)-β-farnesene.[8,24,25] Therefore, the antiviral and anti-inflammatory properties of EOs and its components can be used as a reference for the prevention and treatment of COVID-19. With the emergence of resistance to antibiotics and antiviral drugs in clinical treatment, interests in the application of EOs in anti-infection is increasing in a fast pace. Since EOs are natural and relatively safe, these can act as good substitutes for chemically synthesized antibiotics in the future.

The role of EOs in alleviating chronic diseases

Chronic diseases usually cannot be completely cured, and the long course of the disease would cause irreversible damage to important organs, such as the brain, heart and kidney, which can seriously endanger human health. For example, chronic diseases, such as cerebrovascular diseases and malignant tumors, have become the main causes of death worldwide.[26,27] In a series of studies, researchers have found that EOs and its corresponding components hold the potential in reducing blood pressure,[28–32] regulating blood glucose[10,33] and inhibiting tumor development,[11,34–37] thereby imposing positive effects on the improvement of chronic diseases.

Anti-hypertensive effect of EOs

Various EOs have been reported to have the function of regulating blood pressure through different pharmacological mechanisms. In a clinical trial that recruited 83 pre-hypertensive and hypertensive subjects, it was revealed that inhaling an EO mixture of lavender, ylang-ylang, marjoram and neroli at a ratio of 20:15:10:2 can effectively relieve systolic blood pressure in patients.[28] In other studies, using the rat aortic ring model, it was revealed that EOs obtained from *Alpinia Zerumbet*[29] and *Trachyspermum ammi* Sprague[32] can directly dilate blood vessels and lower blood pressure through the inhibition of calcium influx by acting on calcium channels with independence on endothelial cells. However, the EOs of *Ocimum gratissimum* L. and its main component, eugenol, were found to have vasodilation effects by inhibiting the influx of Ca^{2+} in the plasma membrane through the use of the aortic ring model of DOCA-salt hypertensive rats, which depended on the integrity of the vascular endothelium.[30] Overall, although these above-mentioned EOs exhibit different mechanisms for reducing hypertension, these findings highlight the potential applications of EOs as an alternative therapy in anti-hypertensive treatment.

Anti-diabetes effect of EOs

A variety of EOs can improve and control diabetes by regulating blood sugar. Both *in vivo* and *in vitro* studies have reported that the EO of *Salvia officinalis* L. can significantly inhibit the activity of α-amylase and lipase, thereby reducing the blood glucose concentration and liver glycogen content in male rats with diabetes induced by Alloxan.[10] The important chemical components contained in *Salvia officinalis* L. can be orally administered under the supervision of doctors, and may be a potentially valuable supplement for the treatment of diabetes in the future. Furthermore, the clinical-randomized controlled trial conducted by Shojaei *et al.*, and the results of the population study conducted by the Zabol Diabetes Center revealed that the EO of *Rhubarb* stem (shoot) can effectively reduce the HbA1c level and fasting blood glucose in patients with type-2 diabetes mellitus.[33] Interestingly, some EOs have good therapeutic and preventive effects on both hypertension and diabetes. For example, Oboh *et al.* reported the mechanism by which black *pepper* EO controls and/or prevents type-2 diabetes mellitus and hypertension, which may be due to the inhibition of α-amylase, α-glucosidase and angiotensin converting enzyme activities through the phenolic content and antioxidant activity of the extract.[38,39] Based on the above-mentioned studies, it can be implied that EOs hold a potential as a reservoir for the design and development for anti-diabetic drugs.

Anti-tumor effect of EOs

Some EOs have been reported to have biological activities in cancer treatment. For example, Greay *et al.* applied 10% of the topical melaleuca white (tea tree) oil abundant in terpenes to immunocompetent tumor-bearing mice. They found that tea tree oil can significantly inhibit the growth of invasive, subcutaneous and chemo-resistant tumors in mice, and has antitumor activity *in vivo.*[34] Frankincense EO[35] and Thymus vulgaris L. EO[11] were also identified to induce the apoptosis of tumor cells in *in vivo* and *in vitro* breast cancer models. Xing *et al.* reported that EOs obtained from the leaves of *Erythrina corallodendron* L. can inhibit the proliferation, migration and invasion of breast cancer cells in a dose-dependent manner.[36] Furthermore, a study reported that cinnamaldehyde can inhibit cell growth by inducing apoptosis and reversing the epithelial mesenchymal transition by terminating the Wnt/beta-catenin pathway.[37] All these findings suggest that certain types of EOs should deserve further investigation as adjuvant drugs for treating cancer migration and invasion.

The role of EOs in alleviating mental disorders

EOs usually contains a variety of small aromatic compounds. Some of these are liposoluble, and can easily cross the blood-brain barrier,[40] acting on the central nervous system.[6] Furthermore, studies have revealed that EOs exhibit promising effects in the adjuvant treatment of emotional disorders, such as depression and anxiety, as well as insomnia. Hence, the proper and rational use of EOs can effectively relieve the discomfort caused by anxiety, and significantly improve psychological disorders, such as depression and anxiety (Table 1).[6–8,10,17,18,20,21,30–32,34,36–38,40–53] Clinical trials have revealed that Lasea, the commercial product of lavender EO, can effectively relieve the anxiety level and insomnia disorder of patients with depression.[6] Lasea is orally administered through 80 mg soft gelatin capsules, which is based on the extract of lavender, and mainly includes aloes and linalool acetate. In addition, Lehrner[54] and McCaffrey[55] reported that lavender, orange and rosemary EOs have good effects on anxiety in patients and volunteer participants. At present, the drugs used to treat insomnia usually have different degrees of side effects, as well as problems on drug dependence or resistance. The treatment of insomnia by EO aromatherapy can achieve the effect of improving sleep quality, and this can also be easily accepted by patients.[56,57] A randomized cross-controlled clinical trial revealed that the inhalation of lavender EO can significantly improve the sleep quality, quality of daily life, and mood, of patients with insomnia and diabetes.[58]

Other diseases

As reported by a variety of studies, EOs have anti-allergy, anti-asthma and anti-aging effects. For example, bronchial asthma is a chronic inflammatory disease of the airways, in which a variety of cells and cellular components are involved. The terpene contained in EOs can relax the bronchial smooth muscle,[41] reduce airway inflammation,[42] and inhibit airway remodeling. As a result, EOs have the potential to be used for relieving asthma symptoms

Table 1. Summary of bioactive functions of essential oils in human diseases

Category	Diseases	Essential oils	Plant information (plant parts)	Main compounds	Refs.
Infectious diseases	Virus infection: 1. Yellow fever virus; 2. Herpes simplex virus; 3. Zika; 4. COVID-19	1. *Lippia citriodora*; 2. *Aloysia triphylla*; 3. *Ayapana triplinervis*; 4. *Eucalyptus*	1. *Verbenaceae* (not applicable); 2. *Verbenaceae* (leaves); 3. *Asteraceae* (aerial parts); 4. *Myrtaceae* (aerial parts)	1. Geranial, Neral, Limonene; 2. α-Tujone, cis-carveol, carvone, limonene; 3. Thymohydroquinone dimethyl ether; 4. 1,8-cineole, jensenone	1-44; 2-45; 3-46; 4-8
	Bacterial Infection: Tuberculosis	1. *Piper.diospyrifolium, Piper.aduncum*; 2. Klonemax™ (*Eucalyptus*)	1. *Piperaceae*, *Piper* L. specie, (leaves); 2. *Myrtaceae,* (not applicable)	1. α-thujene, α-pinene, β-pinene, limonene, β-phellandrene, safrole, δ-elemene, β-elemene, γ-elemene, α-humulene, dehydro-aromadendrene, trans-cadina-1(6), 4-diene, γ-gurjunene, bicyclogermacrene, (Z)-α-bisabolene, δ-cadinene, spathulenol, caryophyllene oxide, humulene epoxide II, epi-1-cubenol, epi-α-muurolol and α-muurolol; 2. 1,8-cineole	1-20; 2-21
	Fungal Infection: 1. Dermatophytes; 2. Candidiasis; 3. Skin fungal infections	1. *Artemisia sieberi Besser* (Lotion 10%, twice daily for two weeks); 2. *Eucalyptus*; 3. *Myrrh*	1. *Compositae* family (aerial parts); 2. *Myrtaceae, odorata* specie, (leaves); 3. *Burseraceae* family (aerial parts)	1. α-thujones, β-thujones; 2. 1,8-cineole; 3. Furanoeudesma, 1,3-diene, menthofuran	1-47; 2-7; 3-48
	Protozoan Infection: Leishmaniasis	1. *Artemisia annua* leaves; 2. *Vernonia polyanthes* Less	1. *Asteraceae* (leaves); 2. *Asteraceae* (leaves)	1. Camphor; 2. Zerumbone	1-17; 2-18
Chronic diseases	Diabetes	1. *Salvia officinalis* L.; 2. *Piper guineense*; 3. *Clausena Harmandiana, Clausena Guillauminii, Clausena excavata*	1. *Lamiaceae* (leaves); 2. *Ashanti* black pepper (all); 3. *Citrus* family, *Clausena* specie (leaves)	1. Oxygenated monoterpenes, Hydrocarbon monoterpenes, Hydrocarbon sesquiterpenes; 2. α -Pinene, β-pinene, cis-ocimene, myrcene, Alloocimene, 1,8-cineole; 3. Seselin, terpinen-4-ol	1-10; 2-38; 3-49
	Hypertension	1. *Trachyspermum ammi*; 2. *Ocimum gratissimum* L.; 3. *Alpinia zerumbet*; 4. *Piper guineense*; 5. *Aniba rosaeodora*	1. *Apiaceae* (seeds); 2. *Labiatae* (aerial parts); 3. *Zingiberaceae* (aerial parts); 4. *Ashanti* black peper (all); 5. *Lauraceae* (trunk)	1. Thymol, gamma-terpinene, p-cymene; 2. Eugenol; 3. 1,8-Cineole; 4. α -Pinene, β -pinene, cis-ocimene, myrcene, alloocimene, 1,8-cineole; 5. Linalool	1-32; 2-30; 3-31; 4-38; 5-50
	Tumor: 1. AE17 mesotheliomas and B16-F10 melanomas; 2. Breast cancer; 3. Non-small cell lung cancer	1. *Melaleuca alternifolia*; 2. *Erythrina corallodendron* L. leaves; 3. *Cinnamomum cassia*	1. *Myrtaceae* (leaves); 2. *Erythrina* genus (leaves); 3. *Lauraceae* (not applicable)	1. Terpenes; 2. Linalool; 3. Cinnamaldehyde	1-34; 2-36; 3-37
Mental disorders	Anxiety	1. Lasea™ (*Lavender*); 2. *Pelargonium roseum*	1. *Labiatae* family (flowers); 2. *Geraniaceae* family (leaves)	1. Linalool, linalyl acetate, 1.8-cineole, β-ocimene, terpinen-4-ol and camphor; 2. Monoterpene alcohols citronellol and geraniol	1-6; 2-40
	Depression	1.Lasea™ (*Lavender*); 2.*Reunion Geranium*; 3.*Toona ciliata Roem*. var. yunnanensis	1. *Labiatae* family [flowers]; 2. *Geraniaceae* family[leaves]; 3. *Meliaceae* family[leaves]	1. Linalool, linalyl acetate, 1.8-cineole, β-ocimene, terpinen-4-ol, camphor; 2. Monoterpene alcohols citronellol, geraniol; 3. Estragole, β-elemene, β-cubebene, γ-elemene	1-6; 2-40; 3-51

(continued)

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Table 1. *(continued)*

Category	Diseases	Essential oils	Plant information (plant parts)	Main compounds	Refs.
	Insomnia	1.Lasea™ (*Lavender*); 2. Compound Anshen EO (*Lavender, Sweet orange, Sandalwood, Frankincense, Orange blossom, Rose, Agarwood* oil blend ratio 10:4:2:1.6:1.2:1:0.6)	1. *Labiatae* family (flowers); 2. (not applicable)	1. Linalool, linalyl acetate, 1,8-cineole, β-ocimene, terpinen-4-ol, Camphor; 2. D-limonene, Linalool, Linalyl acetate, α-Pinene, α-Santalol	1-6; 2-52
Other diseases	Asthma	1. *Eucalyptus* oil; 2. *Nepeta cataria* L.; 3. Aromatic spices	1. *Myrtaceae* (not applicable); 2. *Limiaceae* (not applicable); 3. (not applicable)	1. 1,8-cineole; 2. 1,8-cineol, α-humulene, α-pinene and geranyl acetate; 3. Citronellol, α-terpineol, carvacrol	1-21; 2-41; 3-42
	Aging	1. *Pluchea dioscoridis*; 2. *Erigeron bonariensis*; 3. *Coriander*	1. *Asteraceae* (above-ground parts); 2. *Asteraceae* (above-ground parts); 3. *Apiaceae* (fruits)	1. α-Maaliene, berkheyaradulen, dehydro-cyclolongifolene oxide, aromadendrene oxide-2, β-muurolene, and α-eudesmol; 2. Trans-α-farnesene, O-ocimene, isolongifolene-5-ol, α-maaliene, berkheyaradulen, and α-muurolene; 3. Linalool	1-53; 2-53; 3-43

under the supervision of doctors. Furthermore, EOs have been shown to be rich in antioxidants, and have active effects in inhibiting elastase, tyrosinase and hyaluronidase. Therefore, these have potential biological activities in anti-wrinkle effects, and might have a good effect in improving exogenous aging.[43,59] The EOs, main components, and related diseases reported in the literature are listed in Table 1.

Application of network pharmacology in essential oil researches

Network pharmacology was first proposed by Andrew L Hopkins in 2007,[60] which integrates large amounts of information to obtain new discoveries by combining computational and experimental methods. In contrast to the classical "one target, one drug" view, network pharmacology has transformed the previous research framework into a "network target, multi-component therapy" model, in order to study the mechanisms of medicinal herbs and its complex components from a holistic perspective.[61] This is completely consistent with the holistic view of herb-centered complementary therapy.[62] This would allow for the exploration of complex active molecular components and potential molecular targets in herbal formulations, and enable researchers to understand the molecular relationship between different components in a compound, and between components and complex diseases.[63] Pharmacological efficacy benefits from its internally integrated multimolecular systems, resulting in clinically meaningful collective effects. In network pharmacology, a network is a combination of various connections between herbal formulations and diseases. Networks mainly comprise of nodes and edges, in which the nodes represent the genes or any biological entity in a biomolecular network, and the edges represent the association, interaction, or any other well-defined relationship. In practice, the construction, analysis and verification of this network is the general path of network pharmacology research. A complex biological network on top of the vast array of existing databases is initially built. Then, the key nodes in the network are identified, and the key biological processes are predicted through network analysis. Finally, further verification through experiments, molecular docking and other operations is performed to ensure the reliability of the predicted results. At present, various modern tools are used for network pharmacology research, such as disease-target databases: TCMSP and OMIM.[64,65] Active compound databases, such as PubChem[66] and ChEMBL,[67] can also be routinely and interactively used. Biomolecular interaction databases, such as HAPPI[68] and STRING,[69] are essential for the analysis. In addition to these databases, suitable analysis tools, such as CytoScape[70] and GUESS, are required. These tools can more effectively and accurately screen out the active ingredients and targets from EOs, and predict the mechanism of action.[71] In recent years, the mechanisms of traditional herbal medicines, including EOs, in the treatment of various serious diseases have been successfully predicted, including depression,[72] arthritis,[73] diabetes[74] and other diseases,[75,76] and achieved certain results.

EOs are widely used in the form of aromatherapy or phytotherapy. Some of these are used to treat insomnia, depression, Alzheimer's disease (AD), inflammation, asthma, and various other abnormal conditions.[77,78] Although various molecular mechanisms of actions have been proposed for EOs, most studies have only tested purified molecules, and the complex mixtures of compounds in herbal medicines have not been investigated, to date, although these have been shown to have more potent effects, when compared to a single isolated compound.[79] Therefore, there is a need to

develop new methods for assessing the effects of complex mixtures of compounds obtained from Eos.[80] Network pharmacology, as a powerful strategy that considers all potential active ingredients, has unprecedented potential for the holistic study of Eos.[81] This method constructs a plant complex target disease network based on the known molecular targets of experimental bioactive molecules in EOs. Through the characterization of disease-related target networks, the multiple roles of EO components can be rationalized, maintaining the integrity of the active molecular properties of plant complexes, and its use in the treatment or prevention of specific medical conditions.[81] In the analysis of the main components of EOs by network pharmacology, the more a disease targets a certain EO, the more these targets are enriched in the main pathogenic pathways of the disease. This indicates that the component may have a more important role in the treatment of the disease. If different EO components act on a common target or signaling pathway, this indicates that these EO components have synergistic effects in the treatment of the disease.[44]

Various studies have explored the mechanisms by which EOs and its components are used to treat diseases via network pharmacology. For mental disorders, Wang *et al.* used network pharmacology to study the effective components, target proteins and molecular pathways of lavender in the treatment of insomnia. The ingredients of volatile oil obtained from lavender were analyzed by gas chromatography-mass spectrometry, and 906 target proteins of lavender and 182 target proteins of insomnia were predicted by different databases. Furthermore, Kyoto Encyclopedia of Genes and Genomes (KEGG) and Gene Ontology (GO) enrichments were conducted based on the shared parts of the target proteins of lavender, and the target proteins of insomnia. By drawing network diagrams and performing an enrichment analysis, it was found that acetic acid and hexyl ester regulates key target proteins ADRB1 and HLA-DRB1, and interferes with the 5-hydroxytryptamine signaling pathway and GABAergic synapses signaling pathway, playing key roles in the treatment of insomnia.[82] This study expounds the mechanism of lavender in regulating insomnia through multi-target and multi-channel, and provides a scientific basis for further research on the effect of lavender on insomnia. Another study was carried out by Li *et al.* to investigate the mechanism of volatile oil obtained from *Alpinia oxyphylla* for treating AD based on network pharmacology.[83] Six effective components of *Alpinia oxyphylla* were identified by gas chromatography-mass spectrometry, and four potential active ingredients in the treatment of AD and four core targets were screened through the protein-protein interaction network. The GO and KEGG enrichment analysis results revealed that this included nerve ligand receptor interaction, the calcium signaling pathway, cholinergic synapse, and 5-hydroxytryptaminergic synapse. Furthermore, the results indicated that EOs obtained from *Alpinia oxyphylla* can synergistically treat AD by regulating calcium balance, cholinergic balance and phosphorylation.

In addition, Herb Siegesbeckiae (HS) has been widely used to treat inflammatory joint diseases, such as rheumatoid arthritis (RA) and arthritis. However, its molecular mechanisms and active ingredients have not been completely elucidated. Yang *et al.* investigated the multi-target action mechanism and main active components of HS EO in anti-RA, and screened out 31 HS core targets and 16 main active components by network pharmacology. The binding degree of most active components that refer to CSF2 and IL1β exceeded 10 (degree=16), indicating that the prevention and treatment of RA by HS may play a role through the combination of multiple components and multiple targets,[84] It is noteworthy that aromatherapy does not appear to have the side effects of various traditional psychotropic drugs, which clearly deserves further clinical and scientific research.[85]

In recent years, network pharmacology prediction technology has been widely used in the field of herbal medicine due to its systematic and holistic advantages.[13,86,87] It is very important to validate the results of the network pharmacology method.[63] Molecular docking, which is a drug design method based on receptor properties, and interactions between receptors and drug molecules,[88] can confirm the validity of predicted targets based on the docking scores, and binding between the receptor and ligand molecules.[89] As an important technology in the field of computer-assisted drug research, a large number of software and computational web servers have been developed and applied, including DOCK,[90] AutoDock,[91] AutoDock Vina,[92] PyMOL,[93] Protein Database and PubChem (https://pubchem.ncbi.nlm.nih.gov/). Xiao *et al.* investigated the mechanism of turmeric EOs in the treatment of insomnia. They used AutoDock Vina and PyMOL to conduct the molecular docking and visualization of 17 targets, and active components related to sedation and hypnosis, providing useful insights into the mechanism of action of active ingredients.[94] Lu *et al.* used molecular docking to verify the affinity of active compounds in *Artemisia argyi* essential oil for the treatment of pressure injury with core targets by downloading the top 10 core targets and top seven ligand files from the Protein Database and PubChem databases. Then, they used the AutoDock Vina software for molecular docking.[95] The results revealed that the top seven active compounds of *Artemisia argyi* essential oil had good affinity for key targets, and that the root mean square deviation of each docking target and compound was <2 angstroms.[95] In summary, the application of network pharmacology and molecular docking technology can effectively clarify the pharmacodynamic material basis of complex chemical substance systems, and improve the efficiency in drug discovery and development via the EO screening process.[71,96]

Conclusions

Network pharmacology is an integrated approach to efficiently elucidate the molecular mechanisms of EOs in the treatment of various human diseases, such as infectious diseases, chronic diseases, and mental disorders. The present study conducted a review of EOs, from the extraction of plant EOs to the functional application of EOs in human diseases, and subsequently to the network pharmacology of EOs. This provides a timely and brief updated overview of recent studies that involve EOs and human diseases, leading to insights in the potential applications of EOs as a natural reservoir for novel drug development. Overall, it can be concluded that network pharmacology offers a comprehensive and accurate understanding of molecular mechanisms for EOs in the complementary therapy processes of human diseases. This could significantly promote cost-effective natural drug development, and facilitate the popularity of EOs as a complementary medicine.

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Conflict of interest

Liang Wang serves as an editorial board member of Future Integrative Medicine. The authors have no other commercial or financial relationships that could be construed as a potential conflict of interest to disclose.

Author contributions

LW conceived the core ideas of the manuscript, planned the structure of the manuscript, and was responsible for the student supervision and project administration. YDZ, JWT, QHL MG, ZWM and JYM performed the literature review. JWT visualized the literature data. All authors wrote and revised the manuscript. All authors read and approved the final manuscript.

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