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A review on essential oil based therapies as an effective weapon against diseases

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Abstract
Secondary metabolites are produced by higher plants and are engaged in defense mechanisms against herbivores, pests, and diseases. These phytochemicals may also have beneficial effects on the human body, such as antioxidant, anti-inflammatory and anti-microbial characteristics. Due to the exacerbation of new and reemerging infectious diseases, as well as the developing resistance to antibiotics now in clinical use, the pressure to identify and develop novel and effective anti-infectious agents has increased tremendously. One method for controlling diseases caused by bacteria is to use natural bioactive substances that can fight the infection. Essential oils, polyphenols, and glycosidic glucosinolates isolated from numerous species (e.g. medicinal and aromatic plants) have demonstrated promising antimicrobial action against a variety of human infections. In the present review, the cardio-protective, neuro-protective, hepato-protective, and anti-cancerous activity of various essential oils have been discussed with major constituents. EOs have proven to be safe and significantly effective as antioxidant, anti-inflammatory, anti-diabetic, anticancer, anti-hyperpigmentation, anxiolytic, antibacterial, antiviral and antifungal agents.

Keywords: essential oils, chemical composition, hepato-protection, cardiovascular, cancer, neuro degenerative

Introduction

Antimicrobial therapy used to treat several medical conditions has a number of side effects. In addition, long-term usage of these drugs makes microbe resistant to it. Today, the most serious threat to world health is the emergence of microbial resistance to drugs, necessitating the need for a much safer, more effective, and less expensive therapeutic option to aid in disease prevention and treatment [1]. Natural phyto-chemicals derived from plants especially secondary metabolites have been a good alternative to synthetic compounds and are thus considered as a gift from nature to humans [2].

Essential oils (EOs) are highly concentrated, aromatic, volatile, secondary metabolites isolated from raw plant extracts using dry distillation, steam distillation, or a mechanical process that does not include heat. In the traditional sense, these are not oils but they share the same low water solubility as oils. EOs are utilized in food flavoring and perfumery because they have an odor [3]. EOs are typically dense combinations containing hundreds of different odrant components. Of the about 17,000 aromatic plant species belonging to the family Lamiaceae, Verbenaceae, Myrtaceae, Zingiberaceae, Poaceae, Rutaceae, Piperaceae, Asteraceae, Cupressaceae, Lauraceae, and Umbelliferae are the most common EO producers [4]. Table 1 contains a list of medicinal and aromatic plants along with the families that produce EOs. Nowadays EOs are gaining popularity, due to their effective role in pharmaceutical, perfumery and flavor industry. By 2022, the EOs market is expected to reach USD 11.67 billion, with many bioactive formulations including Eugenol-Tween and Eugenol-ethoxylate, Herbalox, ActiVin, and Pycnogenol on the market [5]. Considering the above comprehensive facts, the goal of the present review is to discuss some of the phytochemicals or essential oils that are being used to treat human diseases.

Table 1: Essential oils yielding plants and their families

Family	Plant name
Asteraceae	*Anthem nobilis* (roman chamomile), *Achillea milefolium* (yarrow)
Myrtaceae	*Eucalyptus globulus, E. alba, E. citriodora, E. Propinqua, E. Salgina, E. Robusta, E. Urophylla, Melaleuca alternifolia* (Tea tree), *Syzygium aromaticum* (clove)
Laminaceae	*Lavandula officinalis, Mentha piperita, Rosmarinus officinalis, Thymus vulgarius, Melissa officinalis* (lemon balm), *Salvia officinalis* (sage)
Rutaceae	*Citrus limonum, C. bergamia, C. aurantifolia*
Labiatae	*Ocimum gratissium* (Ram Tulsi), *O. canum* (Dulal Tulsi), *O. basilicum* (Ban Tulsi), *O. kilimandscharicum, O. ammericanum, O. camphora* and *O. sanctum*
Umbilliferae	*Tracyspermum copticum (Ajowan), Anethum sowa, A. graveolens, Cuminum cyminum, Petroselinum sativum, Allium sativum*

Major Components of Essential Oils

EOs are synthesized and stored majorly in secretory parts and epidermal cells of plants. About 85% of these major stored compounds consist of terpenes, terpenoids, aromatic and aliphatic compounds, for instance, limonene and phellandrene make up to 35% in case of Anetheum leaf oil, and 59% menthol and 19% menthone are present in *Mentha piperita* oil. According to study, the main chemicals obtained from the *Aloysia tryphila* EO were geranial, neral, and limonene accounting for 21.83%, 17.45%, and 11.03% respectively. *Thymus valgaris* EO contain 79.15% thymol, 4.63% caravrol and 3.27% *p*-cimene. The *Ocimum* species showed different composition of oils. Thymol was major component of *O. applii* (64.5%) and *O. vulgare* (38.0%), while eugenol was obtained from *O. gratissium* (93.9%) and *O. basilicum* (28%) [7]. A number of factors are responsible for variation in chemical compositions of EOs. Endogenous factors include the plant anatomical, physiological behavior and biosynthetic process of secondary metabolites that may vary in different plant tissues or in different geographical conditions. Over a long period, extrinsic elements might alter some genes accountable for the volatile synthesis, resulting in chemotype or ecotype within the same species of plant.

EOs comprises alcohols, phenols, ketones, aldehydes, amides, amines, amides, and esters, among other volatile chemicals, depending on the chemical class they belong to. The therapeutic effects of EOs are determined by the concentration and content of its constituent chemicals. As a result, they can have a wide range of bioactive properties, such as neuro-protective, cardio-protective, hepato-protective, anti-oxidant, anti-inflammatory, anti-cancer, anti-diabetic, anti-hyperpigmentation, anti-fungal, anti-bacterial, and anti-viral as shown in Fig.1 [8].

Role of EOs in General Health

Anticancer activity of EOs

Cancer is the second leading cause of mortality after heart disease, and is rapidly becoming a global health issue [9]. Besides the fact that there is no effective, precise and safe treatment for majority of cancer; chemotherapy, radiotherapy and surgery are considered as the only available therapy. The majorities of cancer chemotherapy medicines are extremely cytotoxic and target proliferating cell populations. Because these medications are non-discriminatory, they have significant negative consequences in normal cells with a high proliferation index, such as those in the gastrointestinal system and bone marrow, limiting the number of anticancer therapies available [10].

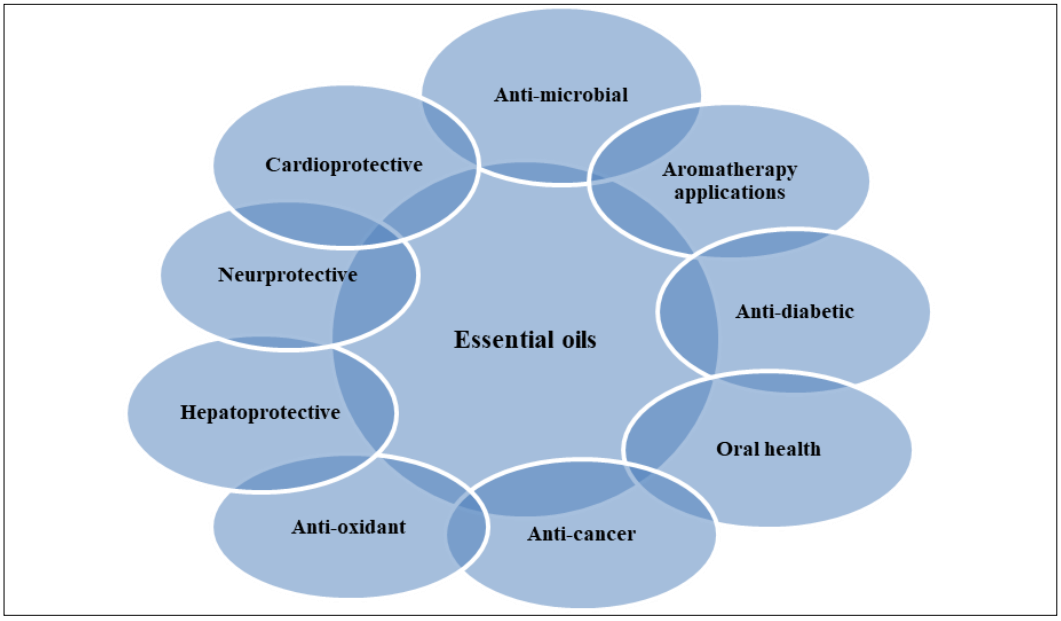

Fig 1: Bioactive properties of Essential oils

As a result, there is a widespread demand for novel medication that are extremely effective, have low toxicity, and have minimal environmental impact. Natural products in fact, play an integral role in preventing and treating the cancer as they have antioxidant and anti-inflammatory activity. Over the last decade, medication development has increasingly concentrated on natural anticancer chemicals extracted from medicinal plants. Traditional medicinal herbs have been utilized for pharmacological and dietary therapy in China, Japan, India, Thailand, and other East Asian countries for millennia, and they are still commonly employed in cancer treatments today [11]. For instance, the volatile components of plants, like *Pistacia lentiscus*, have been used as powerful chemo-preventative agents with high antioxidant and potential anticancer activity [12].

A mechanism-based analysis uncovered that limonene inhibited post-translational isoprenylation and not cholesterol biosynthesis as the path to reducing cell proliferation and cell cycle progression. also, the protein iso-prenylation is inhibited by liquorice and perillyl alcohol. Even though farnesol had no effect on small G-protein prenylation, derivatized versions of farnesol decreased methyl-transferase activity and lowered G-protein

prenylation [13]. In addition to gamma-bisabolol, the sesquiterpene alcohol in *Matricaria chamomilla* is thought to contribute to chamomile's mild anti-inflammatory effect. Since it is nontoxic to animals, cosmetic preparations are frequently made from it. Studies showed that in human and rat glioma cells, the cytotoxic effect of gamma-bisabolol were strongly dose- and time-dependent. The effect of bisabolol on normal glial cells was that it quickly induced apoptosis via the mitochondrial pathway without harmful effects. Gliomas are among the most aggressive malignant tumors, against which no effective and non-toxic treatment has yet been reported; therefore, gamma-bisabolol holds great promise for the treatment of this highly malignant tumor. Daunorubicin and methane sulfonate were also inhibited by the EO of chamomile [14]. Table 2 enlists the plant and its major constituents with their specific anti-cancerous activity.

Table 2: List of Plants and phytochemicals present to suppress specific cancer.

Plant	Phytochemical	Specific cancer suppressed	Suppression	Reference
Allium wallichii	Steroids, flavonoids, terpenoids, glycosides and reducing sugars	Prostate, cervical and breast cancer	*In-vitro*	15
Artemisia annua	Artemisinin	Liver, pancreatic and breast cancer	*In-vitro* and *in-vivo*	16
Camelia sinesis	Epicatechingallate, picatechin, epigallocatechin	Lung, prostate, skin, and breast cancer	*In-vitro* and *in-vivo*	16
Curcuma longa	Curcumin	Colon adenocarcinoma	*In-vitro*	17
C. longa	Curcumin, ascorbic acid	Leukemia, glioblastoma and colon cancer	*In-vitro*	17
Ginkgo biloba	Ginkgetin, ginkgolide A & B	Hepatocarcinoma, prostate, liver and colon ovary cancer	-	16
O. sanctum	Eugenol, orientin, vicenin	Breast, fibrosarcoma and liver cancer	*In-vitro*	16
Peganum harmala	Harmine	Breast cancer	*In-vitro* and *in-vivo*	18
Polygonum cuspidatum	Resveratrol	Liver, colorectal, and skin cancer	*In-vitro*	16
Smilax chinensis	Tannin, saponins and flavonoid	Sarcoma-180 and ascites sarcoma	*In-vitro* and *in-vivo*	16
Xanthium strumarium	Xanthatin	Liver cancer and lymphocytic leukemia	*In-vitro*	16
Zingiber officinale	Gingerol	Ovary, colon, liver cervix, and urinary cancer	*In-vitro* and *in-vivo*	16
Ziziphus jujube	Linoleic acids, triterpenoids	Breast cancer, human Jurkat leukemia T cells	*In-vitro* and *in-vivo*	16
Z. mauritiana	Methyl stearate, α-linolenic acid	Leukemia, liver cancer and human cervical	*In-vitro*	16

EOs in cardiovascular diseases

Cardiovascular diseases (CVDs) are the major cause of death and a significant economic burden. To treat CVDs, a variety of medicines are administered, including antihypertensive, antihyperlipidemic, and antiplatelet therapies. However, these drugs have adverse effects, including bleeding [19].

As a result, attempts are being made to produce new medications consisting of natural ingredients with minimal adverse effects. EOs are employed with anti-oxidant and anti-inflammatory properties, thus demonstrates a variety of biological features in cardiovascular therapeutics. In mouse aortic rings, for example, neroli EO displayed vaso-relaxant action regulated by the ryanodine receptors and NO-soluble guanylyl cyclase pathway. By reducing Ca^{2+} influx into mouse aortic rings, bergamot EO also produced vaso-relaxation. In chronic nicotine-induced hypertension rats, the chemical 1, 8-cineole, which is a major constituent of eucalyptus EO, has anti-oxidative and anti-hypertensive properties [20]. Table 3 demonstrates the various components of EOs and their role in CVD.

Atherosclerosis

Formation of plaque in the artery's innermost layer, the intima, causes atherosclerosis which in turn is because of the increased cholesterol levels in oxidatively damaged low-density-lipoproteins (LDLs) thereby causing reduction in blood flow [20]. Terpinolene, monoterpene hydrocarbon, eugenol, and thymol are some of the aromatic volatile chemicals found in EOs which have been demonstrated to exhibit anti-oxidative effect against LDL oxidation by slowing the oxidation of intrinsic LDL caretonoids. Garlic EO considerably reduced blood cholesterol and triglycerides while significantly increasing high-density-lipoproteins both in healthy individuals as well as in people suffering from coronary heart diseases. Intravenous injection of basil EO (*O. gratissimum*) resulted in a considerable drop in blood pressure and bradycardia [21].

Thrombosis

Thrombosis is frequently linked to platelet activation and the release of eicosanoids. The anti-platelet activity of lavender EO is wide, reducing the aggregation of platelet caused by Adenosine tri-phosphate, collagen, arachidonic acid, and the stable thromboxane receptor against U46619 without inducing bleeding. Linalyl acetate which is found in 36 percent of lavender oil seems to be the primary antiplatelet component. Organo-sulfur components present in onion EO (*Allium cepa*) also suppressed the platelet aggregation and thromboxane production [22].

EOs in hepatoprotection

As liver is the major site of detoxification and xenobiotic processing, it is frequently affected by toxic chemicals, drugs, invading virus and bacteria through ingestion or infection. Treatments for liver problems include pharmacotherapy, surgery, and liver transplantation [23]. All of these treatments have proven to have minimal therapeutic efficacy and are linked to substantial side effects. It's worth noting that therapy with steroids, vaccinations, and antiviral medications is not only effective, but also carries significant risks due to toxicity, especially when used chronically or sub-chronically. There is clearly a compelling need to study novel and alternative wound healing methods in liver diseases. Because the present medical system lacks a reliable liver protective medication, a variety of medicinal plants are recommended for the treatment of liver issues in order to examine the efficacy of hepato-protectants. In this context, medicinal plants offer a rich source of bioactive compounds that could be employed in drug development programs to treat a variety of ailments, including liver injury. Plants play a protective role because of their antioxidative ingredients, which can delay or prevent the production of reactive oxygen species[24]. Nearly 27 plants from 12 families have been examined for their hepato-protective activity which includes Lamiaceae (7 species), Asteraceae (6 species), Umbellifereae (3 species), Apiaceae (3 species), Rutaceae, Anacardiaceae.

Table 3: EO's component and their role in cardiovascular diseases

Essential oil	Major component	Effects	Reference
Aframomum melegueta, A. danielli	Eugenol	Anti-diabetes, anti-oxidation, ACE inhibition	19, 20
Allium cepa, A. sativum	Diallyl-trisulfide	Fibrinolysis	22
Alpinia zerumbet	Diallyl-trisulfide and Terpinen-4-ol	Fibrinolysis, Blood press	25
Aniba rosaeodora	Linalool	Blood pressure reduction, Vasorelaxation	22
Citrus bergamia Risso	d-Limonene	Anti-oxidation, Angiogenesis inhibition	22
Curcuma longa L.	Ar-turmerone	Anti-platelet, Liver function improvement, Lipid improvement, Anti-inflammation, Vasorelaxation	25
Foeniculum vulgare	Anethole	Anti-platelet, Anti-thrombosis, vasorelaxation	22
Lavandula hybrid	Linalyl acetate	Endothelial function improvement, Anti-platelet, Anti-thrombosis	22
Olea	oleic acid	Blood pressure reduction, Endothelial function improvement, Anti-oxidation	22
Syzygium aromaticum	Eugenol	Anti-oxidation, anti-inflammation, Liver function improvement, Lipid improvement	22

Bignoniaceae, Euphorbiaceae, Hypericaceae, Lauraceae, Poaceae, and Zingiberaceae. According to the research, the administration of EO of *Achillea biebersteinii* at a dose of 0.2mL/kg has a significant hepatoprotective activity against CCl4 induced liver damage compared with control. Furthermore, the biochemical assay indicated that this oil contains: 56.3% monoterpene hydrocarbons, 29.2% alfa-terpinene, 22.9% p-cymene, 4.7% terpinen-4-ol, 4.3% of 1,8-cineole, 3.9% of trans-p-menth-2-en-1-ol, 3.1% of the ascaridole, 2.5% of transpiperitone oxide and 2.1% carvacrol. Similarly, the EO of *A. capillaris* was evaluated *in-vivo* by their hepatoprotective activity against CCl4 induced liver damage in mice, by using bio-chemical methods. The results concluded that the administration of the EO of *A. capillaris* at a dose of 50 mg/kg and 100 mg/kg had a potent hepatoprotective effect against CCl4 in-vivo. Indeed, GC-MS analysis indicated that the oil contains 16.2% of citronellol, 13.9% of 1,8-cineole, 12.59% of camphor, 11.33% of linalol, 7.21% of α-pinene, 3.99% of β-pinene, 3.22% of thymol and 2.02% of myrcene. [46]

EOs in neurological disorders

Parkinson's disease, Alzheimer's disease (AD), epilepsy, migraine, trauma, multiple sclerosis, brain tumours, and other neurological disorders results from malnutrition or bad immune responses are examples of central and peripheral nervous system problems [26]. Drugs that inhibit or stimulate enzymes, up- or down-regulate genes, or improve memory or cognition are all common therapeutic options for neurological problems nowadays. It is possible to treat or totally cure neurological problems with medication that uses one or both of the ways described above; however, these medications have adverse effects such as addiction, oxidative toxicity, sedation, withdrawal symptoms, etc.

As a result, the focus has shifted for creating therapeutic and natural ways to treat neurological disorders in the hopes of achieving a complete cure or major symptomatic improvement. Due to their complexity and stability, EO have proven their efficacy in treating neurological disorders beyond the traditional limitations of conventional therapy.

Alzheimer's disease

Cholinergic dysfunction, amyloid peptide deposits, and neuro-fibrillary intra-neuronal tau protein deposits all contribute to synaptic toxicity, oxidative stress, memory loss, and neuron failure and degeneration in Alzheimer's disease. By decreasing oxidative stress or inhibiting cholinesterase, reducing A-β toxicity is one method of symptomatic relief for AD. In this regard, it is hypothesized that EO could be used as a natural treatment for Alzheimer's disease [27].

According to research, exposure of rats (model for amyloid beta toxicity, A1–42) to *Pinus halepensis* EO vapors (1 and 3 percent) showed efficacy in treating Alzheimer's disease. Similarly, an *in-vitro* investigation of EOs of *Centaurea alba* and *C. jacea* demonstrated low to moderate anticholinesterase activity, indicating therapeutic importance [28]. Analysis revealed that the chemical makeup of EO from *C. alba* and *C. jacea* has 18 and 29 components, respectively. Furthermore, for the first time, *in-vitro* tests demonstrating the inhibition of cholinesterase activity or as antioxidants were conducted employing EO from *Prunus domestica L.*, demonstrating that they operate as potent agents for the prophylaxis of Alzheimer's disease. Table 4 summarizes EO derived from various plant sources and its primary ingredients with anticholinesterase and antioxidant effects.

Table 4: Essential oil pro

Plant	Major constituents	Mechanism	References
Hertiacheirifolia (leaves)	α-Pinene, unknown drimeninisomer, monoterpene hydrocarbons, germacrene D and drimenin, sesquiterpene lactones and sesquiterpene hydrocarbons.	▪ Anticholinesterase activity ▪ Antioxidant activity	29
Tetraclinis articulate (leaves)	α-Pinene, calarene, camphor, β-myrcene, camphene, limonene, l-bornyl acetate	▪ Anticholinesterase activity ▪ Antioxidant activity	27
Sideritis albiflora (aerial parts)	Carvacrol,eugenol, thymol, β-cubebene, β-phellandrene linalyl acetate	▪ Anticholinesterase activity ▪ Antioxidant activity	30
Melaleuca citrine (leaves)	α-Pinene, α-terpineol acetate, 1,8-cineole, α-terpineol, o-cymene, limonene	▪ Anticholinesterase activity	31
Ammodaucus leucotrichus (Aerial part)	d-Limonene, perilaldehyde,β-pinene, perillalcohol, α-pinene, 3-carene	▪ Anticholinesterase activity	32
Mentha longifolia (aerial parts)	1,8-Cineole,trans-piperitoneoxide, linalool, menthone, pulegone, piperitenone oxide	▪ Anticholinesterase activity ▪ Antioxidant activity	32
Polygonum hydropiper L. (leaves)	β-Elemene, β-caryophyllene epoxide, cisgeranylacetone, cis-1,3-diisopropenyl-trans-4-vinyl-4- methylcyclohexane, bicyclo[2.2.2]oct-2-ene, 1,2,3,6-tetramethyl and decahydronaphthalene	▪ Anticholinesterase activity ▪ Antioxidant activity	33

Parkinson's disorder

Parkinson's disease (PD) is the loss of dopamine-producing neurons in the substantia nigra pars compacta in the midbrain, is the most common neurodegenerative disease after Alzheimer's disease. In PD, dopamine becomes unavailable, resulting in the loss of nerve transmission and/or neurons, and, as a result, reduced motor function. Apoptosis, oxidative stress, inflammation, and mitochondrial and protein malfunction are some of the other mechanisms that contribute to PD. Recent medications have only provided symptomatic alleviation and have failed to cure the disease. The most common medications are levodopa, anticholinergic drugs, pramipexole, bromocriptine, and others. However, they have side effects such as oxidative toxicity and increased addiction, thus opting for natural therapies with less adverse effects is suggested for PD prevention [34].

Cinnamon (*Cinnamomum verum*) EO contains cinnamic aldehyde, which has anti-inflammatory, antioxidant, and anti-angiogenic properties. Thus, Cinnamon possesses potency in neurodegenerative illnesses, including Parkinson's disease. In reserpine-induced Parkinson's mice, *Eplingiella fruticosa* EO slowed catalepsy onset and reduced striatum membrane lipid peroxide levels [35]. Similarly, *E. fruticosa* EO delayed catalepsy onset and decreased striatum membrane lipid peroxide levels in reserpine-induced Parkinson's mice [35], while Anti-anxiety activity was induced by *E. fruticosa* EO in combination with cyclodextrins, which also improved memory,

inhibited catalepsy onset, decreased oral dyskinesia frequency, and prevented dopaminergic reduction in the striatum and substantia nigra pars compacta.Furthermore, in a 6-hydroxydopamine-induced Parkinson rat model, β-asarone, a key and important ingredient of *Acorus tatarinowii Schott.* EO, demonstrated the potential for behavioral improvement [34]. β-Asarone, can cross through the blood–brain barrier, activated the endoplasmic reticulum stress pathway, resulting in elevated homovanillic acid, 5-hydroxyindoleacetic acid, and homovanillic acid.

Epileptic disorder

Convulsions, seizures, muscle spasms, brief disturbance or loss of consciousness, impaired/loss of neuronal activity, and neurotransmitter imbalance are all symptoms of epilepsy[36]. Antiepileptic medicines have been proposed to treat epilepsy by targeting secondary messengers or receptors of ion channels, glycine, and glutamatergic and GABAergic metabolism [36]. Natural treatments, such as herbal therapies/formulations, particularly EO, have been shown to be effective antiepileptics.

In an attempt to treat epilepsy, *Artemisia persica* EO was examined for its anti-seizure qualities in mice caused by pentylenetetrazol (PTZ), as well as antioxidant and anti-inflammatory properties[37]. The antiepileptic potency of *Annona vepretorum* EO alone and in complex with a carrier -cyclodextrin was studied in a similar way. They investigated EO's preventive properties in mice against PTZ-induced seizures and found that it significantly reduced the duration of tonic-clonic convulsions as well as mortality. Furthermore, the EO exhibited anxiolytic, sedative, and antidepressant properties when examined in rats. In a PTZ-induced rat model, the antiepileptic effects of *Ducrosia anethifolia* EO and its primary component, alpha-pinene, were also investigated[38]. The antiepileptic potential of the study was demonstrated by the delayed, diminished, and attenuated convulsions, as well as a lower mortality rate in the treated rats [38]. According to a study, the beginning of clonic convulsions was substantially delayed, while the onset time of tonic seizures was enhanced, using EO from *Elettaria cardamomum* for the assessment of antiepileptic activity in a PTZ- or electrically generated seizure mouse model. Furthermore, it slowed the tonic extension of the hind limb, indicating its antiepileptic potential. The primary ingredients present in *E. cardamomum* EO were myrcene, 4-terpinen-4-ol, sabinene, terpinyl acetate, and 1,8-cineole. EO from the leaves of *Cinnamosma madagascariensis* was tested for antiepileptic potency in rats induced to have seizures using PTZ in a similar way [39]. The antiepileptic potential of *C. madagascariensis* demonstrated moderate sedation and reduced convulsions. Chemical analysis revealed the existence of significant components in the EO, including - pinene, limonene, linalool, myrcene, oxygenated monoterpenes, and monoterpene hydrocarbons [39].

Migraine disorder

Migraine headaches are the most common sort of migraines which are commonly accompanied by nausea and sensitivity to light and sound [40]. For migraine prevention, a number of medicines are available and recommended. However, it is still not totally under control, necessitating the continued search for natural migraine treatments. EO has demonstrated their efficacy in the treatment of migraines in this endeavor. In a placebo-controlled randomized clinical trial on 50 patients, EO derived from *Pimpinella anisum* was found to provide effective protection against migraine attacks [40]. Compared to the placebo group without EO, the duration and frequency of migraine attacks, as well as the amount of analgesics consumed, were all modestly reduced. In a randomized, double-blind, placebo-controlled, cross-over experiment for migraine therapy, a comparable finding was observed on the first topical use of *Rosa damascene* EO. When compared to a placebo group without EO, the migraine headache severity was modestly reduced in hot type of migraine with no adverse effects. Furthermore, a research on *Lavandula* EO indicates its significant antimigraine capability in 60 patients in a controlled randomized 3-month placebo-controlled double-blind clinical trial [41]. When compared to the placebo group, EO significantly reduced the severity and frequency of migraine headaches while having no negative side effects [41]. In another study, *Angelicae dahuricae* EO showed antimigraine activity in a nitroglycerin (NTG)-induced migraine rat model, with significant reductions in nitric oxide levels in the brain and serum, calcitonin gene-related peptide in plasma, shooting events of the hind legs, scratching of the head, number of head shakes, and an increased endothelial level after EO administration in rats.

Anxiety-related disorders

Anxiety disorders are the most frequent mental illnesses, characterized by fears of unreasonable, unnecessary, persistent, and disoriented feelings that negatively impact one's quality of life [42]. Benzodiazepines and antidepressants, which are only available by prescription and have side effects, are effective treatments for anxiety disorders.Natural medicines, such as aromatherapies containing EO, could greatly alleviate anxiety symptoms in this area. In Swiss mice, for example, *Nectandra grandiflora* EO demonstrated anxiolytic effects [43].

The anxiolytic effect of the *N. grandiflora* EO is linked to GABA a receptor-mediated regulation and suppression of neuronal calcium influx, according to the study. Furthermore, as compared to a placebo group without EO, *Aloysia polystachya* EO and its hydro-ethanol extract significantly reduced anxiety-related symptoms in a placebo-controlled randomised phase 2 clinical trial including 54 people.The active ingredients of *A. polystachya* EO were found to be limonene and carvone after chemical analysis [42].

Depression-related disorders

Depression, often known as mental illness or mood disorder, is defined by a combination of cognitive, physical, and affective symptoms that might lead to suicidality. Antidepressant medicines, which have certain negative effects, are commonly used to treat depression in the majority of instances. Researchers are now concentrating their efforts on finding natural antidepressants with few negative effects. For example, a recent study on *Origanum majorana* EO demonstrated strong antidepressant-like activity, as evidenced by increased climbing and swimming times, as well as reduced immobility time, in a forced swimming test. Furthermore, noradrenergic, serotonergic, and dopaminergic systems were found to play a role in antidepressant-like activity. The EO of *O. majorana* includes 24 chemical components, with high concentrations of terpinene-4-ol, γ-terpinene, and sabinene [45]. Lavender EO was found to have potential for decreasing sadness and anxiety-like behaviour, as well as boosting neurogenesis and increasing dendritic branching, in a recent *in-vivo* study in adult male Sprague Dawley rats. Additionally, the study reports β-ocimene, α-ocimene, o-cymene, alloocimene, terpinen-4-ol, linalool, camphene, caryophyllene, β-pinene, α-terpineol, β-humulene,γ-terpinene, and δ-3-carene as the key constituents of lavender EO demonstrating the potential antidepressant effect. *Citrus sinensis L. Osbeck* EO, in a similar way, has been shown to alleviate depression in a reserpine-administered mouse. They discovered that terpenes, one of the key components of *C. sinensis* EO, had an antidepressant-like effect similar to antidepressant fluoxetine, as evidenced by an increase in locomotor test and a reduction in dyslipidemia. Furthermore, *C. sinensis* EO therapy elevated dopamine and serotonin levels in the brains of mice, implying that the modulation is attributable to dopaminergic and serotonergic systems. In a chronic unpredictable moderate stress mouse paradigm, limonene, the other primary component of *C. sinensis* EO, exhibited antidepressant potential by increasing neurotrophic, neuroendocrine, and monoaminergic levels. Similarly, methyl jasmonate, one of the principal components of *Jasminum grandiflorum* EO, has been attributed antidepressant efficacy due to its participation in the dopaminergic, noradrenergic, and serotonergic systems[45].

Conclusion

Various treatment strategies encounter barrier which includes increased disease occurrence, side effects of chemical and synthetic drugs, and expensive treatments as in case of cancer therapeutics and safety issues. EOs have been used in the traditional medicine practices since centuries, and several studies have strategized the effectively of EOs against several diseases. In the present review, phytochemicals and therapeutic characteristics along with the methods of applications of EOs in the treatment of acute and chronic disorders were analyzed. Most EOs consists of two to three major phytochemicals for maximum efficacy such as carvacrol and thymol combination, and cinnamaldehyde and eugenol combination. EOs have been found to be consisting of several other bioactive components which are effective against cardiac, pulmonary and neurological disorders. EOs have proven to be safe and significantly effective as antioxidant, anti-inflammatory, anti-diabetic, anticancer, anti-hyperpigmentation, anxiolytic, antibacterial, antiviral and antifungal agents. As most of the studies have been done in animal models, research methodologies should be focused further ahead on conducting clinical trials in humans for evaluating the effective doses and safety recommendations of EOs.

Conflict of interest

The authors have declared that there is no conflict of interest.

References

1. Sun J. The Repurposing of Pharmaceutical Agents to Improve Treatment Outcomes in Antibiotic-Resistant Bacterial Infections. University of California, San Diego, 2018.
2. Cragg G M, and Newman D J. Natural products: a continuing source of novel drug leads. *Biochimica et Biophysica Acta (BBA)-General Subjects*,2013:1830(6):3670-3695.
3. Bhardwaj K, Islam MT, Jayasena V, Sharma B, Sharma S, Sharma P *et al*. Review on essential oils, chemical composition, extraction, and utilization of some conifers in Northwestern Himalayas. *Phytotherapy Research*,2020:34(11):2889-2910.
4. Reddy DN. Essential oils extracted from medicinal plants and their applications. In *Natural bio-active compounds*. Springer, Singapore, 2019, 237-283.
5. Mihai AD, Chircov C, Grumezescu AM, Holban AM. Magnetite Nanoparticles and Essential Oils Systems for Advanced Antibacterial Therapies. *Int. J. Mol. Sci*,2020:21(19):7355.
6. Bilia AR, Guccione C, Isacchi B, Righeschi C, Firenzuoli F, Bergonzi MC. Essential oils loaded in nanosystems: a developing strategy for a successful therapeutic approach. *Evidence-Based Complementary and Alternative Medicine*, 2014.
7. Chouhan S, Sharma K, Guleria S. Antimicrobial activity of some essential oils — present status and future perspectives. *Medicines*,2017:4(3):58.
8. Khanal H, Joshi RK, Upadhyay A. A Review of an Ayurvedic Polyherbal Formulation Mustadi Kwatha. *J. drug deliv. ther*,2020:10(5-s):267-272.

9. Moga MA, Dimienescu, Arvatescu OG, Mironescu CA, Dracea L, Ples L. The role of natural polyphenols in the prevention and treatment of cervical cancer-An overview. *Molecules*,2016:21(8):1055.
10. Bhalla, Gupta YVK, Jaitak V. Anticancer activity of essential oils: a review. J. Sci. *Food Agric*,2013:93(15):3643-3653.
11. Moga MA, Dimienescu OG, Arvatescu CA, Mironescu A, Dracea L, Ples L. The role of natural polyphenols in the prevention and treatment of cervical cancer—An overview. *Molecules*,2016:21(8):1055.
12. Shmuely H, Domniz N, and Yahav J. Non-pharmacological treatment of *Helicobacter pylori*. World *j.gastrointest. pharmacol. therap*,2016:7(2):171.
13. Jeong A, Suazo KF, Wood WG, Distefano MD, Li L. Isoprenoids and protein prenylation: implications in the pathogenesis and therapeutic intervention of Alzheimer's disease. *Crit. Rev. Biochem. Mol. Biol*,2018:53(3):279-310.
14. Gilca M, Tiplica GS, Salavastru CM. Traditional and ethnobotanical dermatology practices in Romania and other Eastern European countries. *Clin. Dermatol*,2018:36(3):338-352.
15. Bhandari J, Muhammad B, Thapa P, Shrestha BG. Study of phytochemical, anti-microbial, anti-oxidant, and anti-cancer properties of Allium wallichii. BMC *Complement Altern. Med*,2017:17(1):1-9.
16. Iqbal J, Abbasi BA, Mahmood T, Kanwal S, Ali B, Shah SA *et al*. Plant-derived anticancer agents: A green anticancer approach. *Asian Pac. J. Trop. Biomed*,2017:7(12):1129-1150.
17. Ooko E, Kadioglu O, Greten HJ, Efferth T. Pharmacogenomic characterization and isobologram analysis of the combination of ascorbic acid and curcumin-two main metabolites of Curcuma longa—in cancer cells. *Front. Pharmacol*,2017:8:38.
18. Ayoob I, Hazari YM, Lone SH, Khuroo MA, Fazili KM, Bhat KA. Phytochemical and cytotoxic evaluation of peganum harmala: structure activity relationship studies of harmine. Chemistry Select,2017:2(10):2965-2968.
19. Rouhi-Boroujeni H, Heidarian E, Rouhi-Boroujeni H, Deris F, Rafieian-Kopaei M. Medicinal plants with multiple effects on cardiovascular diseases: A systematic review. Curr. Pharm. Des,2017:23(7):999-1015. 2017.
20. Seol GH, Shin YK. Essential Oils and Factors Related to Cardiovascular Diseases. Potential of Essential Oils, 2018, 129.
21. Lajis AFB, Ismail NH. Therapeutic application of herbal EOand its bioactive compounds as complementary and alternative medicine in cardiovascular-associated diseases, 2020.
22. Abdollahi M, Salehnia A, Mortazavi SHR, Ebrahimi M, Shafiee A, Fouladian F *et al*. Antioxidant, antidiabetic, antihyperlipidemic, reproduction stimulatory properties and safety of EO of Satureja Khuzestanica in rat in-vivo: a toxicopharmacological study. Med. Sci. Monit. Basic Res,2013:9(9):BR331-BR335.
23. Monisha R. Evaluation of Hepatoprotective and Antioxidant Effect of Girardenia Zeylanica Dcne Leaf Extract Against Ccl4 Induced Liver Damage in Rats, 2014.
24. Prasad S, Gupta S C and Tyagi A K. Reactive oxygen species (ROS) and cancer: Role of antioxidative nutraceuticals. Cancer letters,2017:387:95-105.
25. Shuaib A, Rohit A, Piyush M. A review article on essential oils. J. Med. Plants Stud, 4, 237-240, 2016
26. Tarulli A. Neurology: a clinician's approach. Springer Nature, 2020.
27. Postu PA, Sadiki FZ, El Idrissi M, Cioanca O, Trifan A, Hancianu M *et al*. Pinus halepensis EOattenuates the toxic Alzheimer's amyloid beta (1-42)-induced memory impairment and oxidative stress in the rat hippocampus. Biomed. Pharmacother,2019:112:108673.
28. Politeo O, Carev I, Veljaca A. Phytochemical composition, antiradical and anticholinesterase potentials of Centaurea alba and Centaurea jacea volatile oils. Croat Chem Acta,2019:92:1-5.
29. Rahali N, Younsi F, Boussaid M, Messaoud C. Chemical variability of Hertiacheirifolia (L.) Kuntze essential oils and incidence on antioxidant and anticholinesterase activities. J. Essent. Oil Res,2020:32(1):48-58.
30. Deveci E, Tel-Çayan G, Duru ME, Öztürk M. Phytochemical contents, antioxidant effects, and inhibitory activities of key enzymes associated with Alzheimer's disease, ulcer, and skin disorders of Sideritisalbiflora and Sideritisleptoclada. J. Food Biochem,2019:43(12):e13078.
31. Petrachaianan T, Chaiyasirisuwan S, Athikomkulchai S, Sareedenchai V. Screening of acetylcholinesterase inhibitory activity in EO from Myrtaceae. Thai J. Pharm. Sci,2019:43(1):63-68.
32. Sadaoui N, Bec N, Barragan-Montero V, Kadri N, Cuisinier F, Larroque C *et al*. The EO of Algerian Ammodaucus leucotrichus Coss. Dur. and its effect on the cholinesterase and monoamine oxidase activities. Fitoterapia,2018:130:1-5.
33. Sadiq A, Mahmood F, Ullah F, Ayaz M, Ahmad S, Haq FU *et al*. Synthesis, anticholinesterase and antioxidant potentials of ketoesters derivatives of succinimides: a possible role in the management of Alzheimer's. Chem. Cent. J,2015:9(1):1-9.
34. Nikolova G, Karamalakova Y, Kovacheva N, Stanev S, Zheleva A, Gadjeva V. Protective effect of two essential oils isolated from Rosa damascena Mill. and Lavandula angustifolia Mill, and two classic antioxidants against L-dopa oxidative toxicity induced in healthy mice. *Regul. Toxicol. Pharmacol*,2016:81:1-7.

35. Beserra-Filho JI, de Macêdo AM, Leão AH, Bispo JMM, Santos JR, de Oliveira-Melo AJ *et al* plingiellafruticosa leaf EO complexed with β-cyclodextrin produces a superior neuroprotective and behavioral profile in a mice model of Parkinson's disease. *Food Chem Toxicol*,2019:124:17-29.
36. Pradhan J and Panchawat S. Herbal therapies for epilepsy: chemistry, biology and potential applications of selected plants and compounds. *Chem Biol Interface*,2018:8:205-224.
37. Daneshkhah M, Setorki M. Protective effects of Artemisia persica EOagainst pentylenetetrazol-induced seizure in male mice with emphasizing its mechanism of action. *Iran Red Crescent Med J*,2019:21(2):e85021.
38. Zamyad M, Abbasnejad M, Esmaeili-Mahani S, Mostafavi A, Sheibani V. The anticonvulsant effects of Ducrosiaanethifolia (Boiss) EOare produced by its main component alpha-pinene in rats. *Arquivos de neuro-psiquiatria*,2019:77:106-114.
39. Rakotosaona R, Randrianarivo E, Rasoanaivo P, Nicoletti M, Benelli G, Maggi F. Effect of the leaf EO from Cinnamosma madagascariensis Danguy on pentylenetetrazol-induced seizure in rats. *Chem Biodivers*,2017:14:e1700256.
40. Mosavat SH, Jaberi A R, Sobhani Z, Mosaffa-Jahromi M, Iraji A, and Moayedfard A. Efficacy of Anise (Pimpinella anisum L.) oil for migraine headache: A pilot randomized placebo-controlled clinical trial. J Ethnopharmacol,2019:236:155-160.
41. Rafie S, Namjoyan F, Golfakhrabadi F, Yousefbeyk F, Hassanzadeh A. Effect of lavender EOas a prophylactic therapy for migraine: A randomized controlled clinical trial. *J. Herb. Med*,2016:6(1):18-23.
42. Carmona F, Coneglian FS, Batista PA, Aragon DC, Angelucci MA, Martinez EZ *et al*. Aloysiapolystachya (Griseb.) Moldenke (Verbenaceae) powdered leaves are effective in treating anxiety symptoms: a phase-2, randomized, placebo-controlled clinical trial. *J Ethnopharmacol*,2019:242:112060.
43. Ottman N, Ruokolainen L, Suomalainen A, Sinkko H, Karisola P, Lehtimäki J *et al*. Soil exposure modifies the gut microbiota and supports immune tolerance in a mouse model. *J Allergy Clin Immunol*,2019:143(3):1198-1206.
44. Postu PA, Gorgan DL, Cioanca O, Russ M, Mikkat S, Glocker MO *et al*. Memory-Enhancing effects of Origanum majoranaeoin an alzheimer's amyloid beta1-42 rat model: a molecular and behavioral study. *Antioxidants*,2020:9(10):919.
45. Umukoro S, Adebesin A, Agu G, Omorogbe O, Asehinde SB. Antidepressant-like activity of methyl jasmonate involves modulation of monoaminergic pathways in mice. *Adv Med Sci*,2018:63(1):36-42.
46. Gao Q, Zhao X, Yin L, Zhang Y, Wang B, Wu X *et al*. The essential oil of Artemisia capillaris protects against CCl4-induced liver injury in vivo. Revista Brasileira de Farmacognosia,2016:26:369-374.