A Reassessment on Essential Oils

[1]Ravikant Singh, [2]Ashutosh Pathak, [3]Sharad kumar Tripathi, [4]Anupam Dikshit, [5]Rohit K. Mishra

[1,3]Research Scholar, [2]Assitant Professor, [4]Professor and [5]Associate Professor
[1, 5]Dept. of Biotechnology, Swami Vivekanand University, Sagar-470228, M.P. India
[2, 3, 4]Biological Product Laboratory, Department of Botany, University of Allahabad, Allahabad-211002, U.P. India

***Abstract*: Gymnosperm include many evergreen trees and shrubs which are extremely captivating because of their graceful habit and attractive shapes. Gymnosperms are highly important in forestry and different industries like timber, resin, essential oils, edible nuts etc. Essential oils (EOs) are popularly known as secondary metabolites. EOs are extracted from plants by steam distillation. Compounds generally have low molecular weight. α-pinene, β-pinene, terpenoids, 3-carene, myrcene, sabinene, camphene, and phenylpropanoids exhibit biological properties, which are major constituents of EOs. EOs are involved in various traditional system of medicine to cure cancer, diabetes, inflammation, bacterial and viral diseases. In the current review, we are trying to cover the potential uses of essential oils of angiosperm and gymnosperms.**

***Keywords*: Gymnosperm, Essential oils.**

Introduction

P. roxburghii Sarg. is the native of Himalaya and distributed throughout India, Nepal, Bhutan and Pakistan. *P. roxburghii* is a large tree attaining up to 28-55 m in height with a trunk diameter reaching up to 2 m. The cones of *P. roxburghii* are ovoid, conic and usually open up to 18-20 cm to release the seeds (1). *P. roxburghii* oil has been traditionally used to treat cuts, wounds, boils and blisters (2). In addition, phytochemical screening of Pinus needles and stems have pound abundant amounts of vitamin C, tannins, and alkaloids while the stem has been primarily used as a source of turpentine oil (3-5). *J. communis* L. (known as common Juniper; family Cupressaceae) distributed throughout the cool temperate Northern Hemisphere including America, Europe and Asia. The essential oil, infusions, decoctions, and alcoholic
extracts are used in different fields (pharmaceuticals, alcoholics, etc.) (23, 24). Essential oils are normally used in food products, drinks, perfumes and cosmetics as flavouring agent (6-8). Production of larger amount of EOs indicates the increased consumption of estimated value of 700 million US dollar (17). Chemical composition of EOs may be affected by many factors like genetic variation, plant variety, use of fertilizers, plant nutrition, geographic location of the plants, climate, seasonal variations, and stress. Post harvest management of the plants can also affect the chemistry of EOs. Essential oils can be extracted by steam distillation and have low molecular weight (18). α-pinene, β-pinene, terpenoids, 3-carene, myrcene, sabinene, camphene, phenylpropanoids monoterpenes and sesquiterpenes are the major constituents of EOs (3-5,19). EOs are being used in many traditional systems by human being from ancient times but nowadays characterization of synergistic effect of EOs can also be done (20). Sometimes bioactivity of a specific EO can be decided by either one or two of its components (20). Efficiencies of various EOs can be measured in terms of minimum growth inhibitory concentrations (MICs) (10-12), MIC50, IC50 (10-12) and LD50 recommended by Clinical Laboratory Standards Institute (CLSI). Different strains of pathogens enhance their capacity against drugs and became resistant strain, so people try to switch to alternate methods including the use of EOs. Secondary metabolites constitute complex mixture of EOs and can be synthesized by plants during stresses like insect pest attack, excessive heat, drought etc. These metabolites have excellent chemothereupatic properties against several infectious and non-infectious diseases (21, 22). Essential oils are secondary metabolites that are natural, volatile, complicated compounds characterised by an odour (10-12). In India, this extraction can be done since sacred writing periods (Vedic periods). EOs are volatile liquid, seldom colored (usually straw or yellow coloured) (10-12), lipid soluble and soluble in organic solvents with a usually lower density than that of water. Most of the commercial essential oils are chemotyped by gas chromatography and mass spectrometry analysis (GC-MS) (1-5).

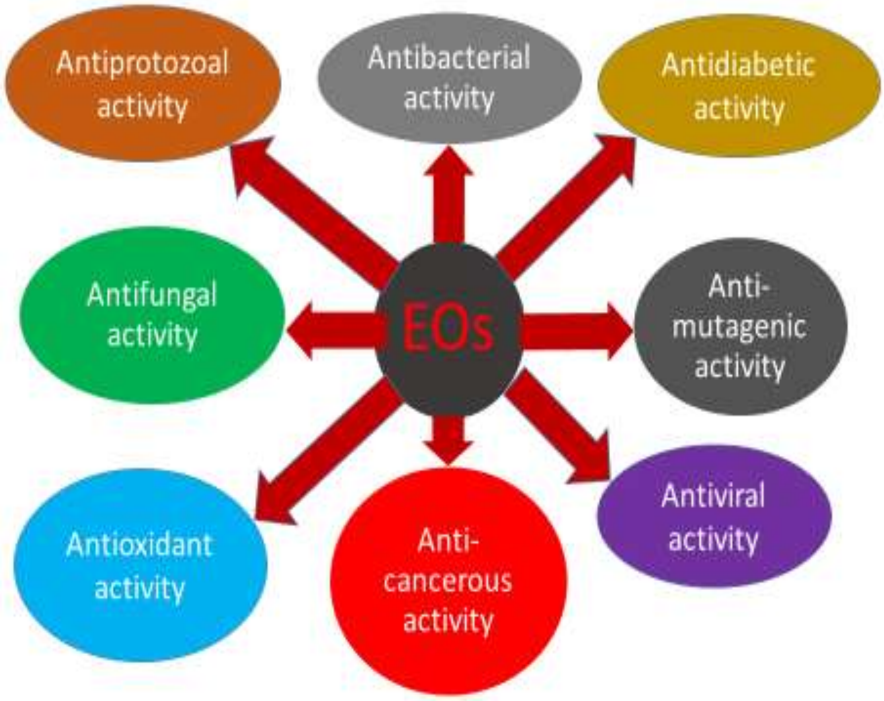

Figure – Showing potential application of EOs.

Taxanomy of essential oil producing plants

EOs producing plants belongs to various genera of different families. Some selected families are known for their ability to produce EOs of medicinal and industrial value. These are Alliaceae, Apiaceae, Asteraceae, Cupressaceae, Lamiaceae, Myrtaceae, Pinaceae, Poaceae and Rutaceae (Table 1) (10-12, 31). Terpenoids are major element of most of the EO producing plant families Whereas, phenylpropanoids more frequently found in plant families like Apiaceae (Umbelliferae), Lamiaceae, Myrtaceae, Piperaceae and Rutaceae. Family Lamiaceae is well known for its aromatic property and EOs of this family is of great commercial use. For example, *Coriandrum*. *Mentha piperita*, *Rosmarinus officinalis*, *Ocimum basilicum*, *Salvia officinalis*, *Origanum vulgare*, *Melissa officinalis*, *Satureja hortnsis*, *Thymus vulgaris* and *Lavandula angustifolia* produces EOs of commercial value (8). *Cinnamomum verum* is well known member of Lauraceae family, produces eugenol riched cinnamon oil. It displays antimicrobial and anticancer potential. EOs with well known antibacterial, antifungal, antitumor, anticancer and antiviral properties have been reported from the family Myrtaceae. For example, *Eucalyptus globulus*, *Melaleuca alternifolia*, *Syzygium aromaticum* and *Myrtus communis* (8). Members of Poaceae are also known to produce EOs like, lemongrass oil (from *Cymbopogon citratus*), citronella oil (from *C. nardus*) and palmarosa (*C. martinii*) oils. The medicinally active portions of those EOs like citral, geraniol and geranyl acetate show antimicrobial and malignant neoplasm properties. Citrus oils that represent terpene and essential oil are derived from the fruit that belong to the Rutaceae family. These parts exhibit antimicrobial potential. The plants *Pelargonium graveolens* of family geranium posses geranium oil whereas *Santalum spp*. of Santalaceae posses sandalwood oil as EOs (6).

Essential oils as antibacterial agents

Plant molecules are wellknown for their antimicrobial properties. EOs shows broad spectrum of activities against numerous Gram positive and Gram negative bacterial pathogens (Table 2) (7, 10-12). The antibacterial activity may vary with oil components as well as different bacterium. For example, sandalwood, manuka oil (*Leptospermum scoparium*) and vetiver (*C. zizanioides*) oils, are extremely active against Gram positive bacteriua, however don't have activity against Gram negative (32). Pseudomonas aeruginosa exhibit tolerance to inhibition by plant EOs as compared to others. Generally, tea-tree, thyme, oregano, cinnamon, lemon grass, bay, clove and rosewood oils are the most active antimicrobials. They are active at concentrations more than 1% vol/vol i.e. exhibit MICs of more than 1% (32). Lemon grass, bay, clove and thyme inhibit growth of *Escherichia coli* at concentrations of 0.02, 0.04, 0.06, 0.05 and 0.05%, respectively (10, 32). In few cases a major constituent molecule has been observed to possess activity better than the EO. For example, carvacrol and eugenol from *S. aromaticum* (clove) oil or terpinen-4-ol in *M. alternifolia* (tea tree) oil display greater efficacy than particular oil. Generally, EOs with phenolics and aldehydes exhibit better antibacterial efficacies (19). Primary mode of action of EOs is the membrane destabilization. Essential oils are lipophilic in nature and hence easily permeable through the cell wall and cell membrane. Interactions of EOs and their components with polysaccharides, fatty acids and phospholipids make the bacterial membranes more permeable, so that loss of ions and cellular contents leads to cell death (33). Similarly, interference in proton pump activity, loss of membrane integrity, leakage of cellular contents can result in loss of viability (34). Other important mechanisms of action include, denaturation of cytoplasmic proteins and inactivation of cellular enzymes leading to bacterial cell death (8). Some gymnospermous essential oils are also found to be very effective against many bacteria like *E. coli*, *Salmonella typhimurium*, *Vibrio cholerae* (10-12).

Antifungal activities of essential oils

Fungi are eukaryotic organism and hence became very hard to hit them. Species like *Candida* spp., *Aspergillus* spp., *Cryptococcus* sp. are notorious and cause trouble for a large population of immunocompromised patients. There are limited options of drugs available for successful antifungal chemotherapy (35). Various, plant and human pathogenic fungi, including yeasts are found to be susceptible to EOs (Table 3) (9, 13-15, 26). The efficiency of inhibition varies with the target organisms and the oil tested. For example, a few members of Apiaceae family show variable anti-candida activity, highest anti-candida activity can be shown by coriander followed by anise, while fennel show least; with the MICs of 0.25%, 0.5% and 1%, respectively (32). Generally, *Cymbopogon* sp. shows better activities against pathogenic yeast (30). EOs of cinnamon, lemongrass, Japanese mint, ginger grass, herbaceous plant and clove oils were discovered as most promising against *C. albicans*. Growth of dermatophytes and also their reproductive structure development is suppressed promptly with EOs rich in phenylpropanoids like eugenol and the monocyclic sesquiterpene alcohols such as bisabolol. Growth and mycotoxin production in moulds like *Aspergillus flavus* is prevented by EOs of plant origin (9, 36). Lemongrass (*C. citratus*) oil is one of the most effective oils against filamentous fungi with the active concentrations ranging from 0.006 to 0.03%. Orange, lemon, mandarin and grapefruit oils inhibit *Aspergillus niger*, *A. flavus*, *Penicillium verrucosum* and *P. chrysogenum* at lower concentration. Drug sensitive as well as resistant pathogenic yeasts, including the major pathogen of humans, *C. albicans*, were inhibited by terpenoid rich EOs (9, 13, 15, 19, 26, 27). Essential oils also possess cell cycle inhibitory activities against *C. albicans*. For example, citral, citronellol, geraniol and geranyl acetate which are the major constituents of eucalyptus oil, tea tree oil and geranium oil are reported to block *C. albicans* in S phase of cell cycle (13, 19). Abnormalities in membrane fluidity result in leakage of cytoplasmic contents and loss of viability of fungi. For example, membrane permeability and respiratory chain activity in *C. albicans* cells is prevented in presence of tea tree oil to result in cell death (19). **Cancer preventive properties**

Treatment of malignant cell growth leading to cancer is one the most tedious task to complete successfully. Plant molecules like taxol are effective against cancerous cell proliferation. Treatment with plant EOs to various types of malignancies shows significant effect. Hence such molecules are supposed to have potential anticancer activities to be useful in prevention and therapeutics strategies (33). For example, geraniol from *Cymbopogon martini* (i.e. palmarosa oil), is reported to interfere with membrane functions, ion homeostasis as well as cell signalling events of cancer cell lines. It is found to inhibit DNA synthesis and reduce the size of colon tumours (37). Eudesmol, a constituent of Atractylodes lancea oilmay find use in prevention of malignant tumours (38). Constituents like terpenoids and polyphenol constituents of EOs prevent tumour cell proliferation through necrosis or induction of apoptosis (40). A great hepatoprotective activity have been reported for *Myristica fragrans* (nutmeg) oil (48), which contains myristicin. EOs exhibit capacity to act as antioxidants and interfere with mitochondrial functions of mammalian cells. As a result, EOs diminish metabolic events (for example, increased cellular metabolism, mitochondrial overproduction and permanent oxidative stress) characteristic of malignant tumour development (37).

Antimutagenic properties

Antimutagenic activities have also been observed in many EOs and their components (47). UV induced mutations in *S. typhimurium*; *E. coli* and *S. cerevisiae* are prevented by EO of *S. officinalis* and its major components (39). EOs of some plants are active against the urethane-induced mutations in *Drosophila melanogaster* like *Helichrysum italicum*, *Ledum groenlandicum*, *Cinnamomum camphora* and *Origanum compactum* (49). Similarly, protection of chromosomal damage in human lymphocytes can also be shown by the extract mixture of *Curcuma longa*, Piper betel and *Acacia catechu* (50). EOs may have ability to inhibit penetration of mutagens inside the cells. Interference with mutation inducing DNA repair systems (39) and induction of necrosis/apoptosis leading to cellular death are among the proposed mechanisms behind antimutagenic activity of essential oils (40).

Essential oils as antioxidants

Essential oils also exhibit free radicals scavenging activity. Oxidative damage has been related to various health problems such as ageing, arteriosclerosis, cancer, Alzheimer's disease, Parkinson's disease, diabetes and asthma (33). Cellular balance of free radicals is mantained by different antioxidants. Flavonoids, terpenoids and phenolic constituents of EOs exhibit significant antioxidant effects (51). Thuja oil show free radical scavenging activity on stable 2,2-diphenyl-1-picryl hydrazyl radical. This plant oil exhibited prominent DPPH free radical scavenging activity of 49.8% in comparison to ascorbic acid and α-tocopherol standard which showed the activity of 67.95 and 71.2%, respectively (46). Free radical scavenging activity have also been reported in *Achillea millefolium*, *Curcuma zedoaria*, *Salvia cryptantha* and *S. multicaulis*, *M. officinalis*, *M. alternifolia*; Ocimum sp. and Mentha sp. (6, 52, 53). Thymol and carvacrol are two main ingradients of EOs of *Thymus* and *Origanum* respectively, act as strong antioxidants (53). Potent antioxidant activity have been shown by *A. sativum*, *A. cepa*, *C. sativum*, *Cuminum cyminum* and *Petroselinum sativum*. Overall, the order of efficacy among the essential oils with good radical-scavenging and antioxidant properties is in the order, clove > cinnamon > nutmeg > basil > oregano > thyme (51).

Antidiabetic potential of essential oils

Hyperglycemic or hypoglycemic condition characteristic of diabetes arise as a result of inability to either produce insulin or use it to regulate normal glucose levels in the blood. Various plant molecules have been analyzed for their antidiabetic potential (44). Comparatively, less information is available on diabetic preventive efficacy of plant EOs (54). Selected EOs are reported to exhibit preventive effects on diabetes associated health hazards (45). A rat model has shown the efficiency of synergistic combination of cinnamon, cumin, fennel, oregano and myrtle oils to enhance insulin sensitivity in type 2 diabetes. The study also reported lowering of blood glucose after treatment of the abovementioned combination of EOs (55). Similarly, *Satureja khuzestanica* oil causes significant decrease in fasting blood glucose levels in diabetic rats (43). Exact mechanism involved behind antidiabetic potential of EOs are still under investigations.

Essential oils as antiprotozoal agents

Various protozoal diseases such as chagas disease, amoebiasis, leishmaniasis, giardiasis, trichomoniasis and malaria, caused by *Trypanosoma cruzi*, *Entamoeba histolytica*, *Leishmania* sp., *Giardia lamblia*, *Trichomonas vaginalis*, and *Plasmodium* sp., respectively, are important public health problems. Use of available antiprotozoal drugs is limited due to drawbacks such as side effects, emergence of drug resistance and requirement of prolonged use (42). Hence new options for treatment of protozoal diseases are being searched. Protozoal diseases can be cured EOs from ancient times (42). These activities have been confirmed with the modern scientific approaches. For example, oregano (*O. vulgare*), herb and *Lippia alba* oils are known to inhibit the expansion of trypanosomal parasite by inflicting cell lysis. *Thymus vulgaris* and its major element thymic acid are shown to possess anti-trypanosomal activity through destabilization of cell wall (56). Compared to others, oils of *C. citrates* and *O. gratissimum* showed better antitrypanosomal activity. *Allium sativum* and *T. vulgaris* oils are known to inhibit *E. histolytica*. EOs and phenolic constituents of *Melaleuca alternifolia*, *Carum copticum* and *L. angustifolia* shows antiprotozoal effects (19). *Cymbopogon citrates*, *Origanum* spp., *Lippia multiflora*, Ocimum gratissimum and *Satureja thymbra* oils shows antimalarial potential (58). EOS of *Achillea millefolium*, *Artemisia abrotanum*, *Chenopodium ambrosioides*, *Croton cajucara*, *C. citrates*, *O. gratissimum*, *Pinus caribaea*, Piper sp. were found to be effective against leishmania (57).

Toxicity issues

Cell can be targeted at multiple sites by essential oils as they have many constituent bioactive molecules (41). Their primary target is cytoplasmic membrane. Disruption and permeabilization of cell membrane leads to loss of important cellular functions such as ion homeostasis and electron transport chain (40). Essential oils can exert cytotoxic effects on eukaryotic cells. Permeabilization of outer and inner mitochondrial membranes causes the cell death by necrosis and apoptosis (59). Alcohol, aldehydes and phenolic constituents are responsible for the cytotoxicity which were used chemotherapeutically against a variety of virus, bacteria and fungi (8, 15, 41). Medicinal use of EOs have some boundaries because of the risk of various toxic effects such as irritation and corrosiveness, sensitization of cells, sever toxicity to organ system, phototoxicity, carcinogenicity, and teratogenicity. Not many reports are available to tackle this complex question. Toxicity profiling for each EO should be done, but this is difficult to carry out, since the toxicity of a particular EO may vary according to composition, which itself is decided by many interdependent factors (31). Efforts are being done to evaluate the toxicity of selected components of EOs, so that they can be used as standards to ensure the safe use. Some times only a single major component isolated from the EO is analyzed. The toxic effects of ketone terpenoids are known since a long time. Estragol have carcinogenic effect which is present in the essential oils of tarragon, star anise, green anise, basils and fennels. When ingested or administered intraperitoneally it causes DNA damage in mice. Similar results have been obtained for methyl iso-eugenol. Essential oil of *M. pulegium* with pulegone and menthofuran as major components has hepatotoxic effect in mice (31). Limonene present in the essential oils of citrus fruits has been evaluated as hepatotoxic after acute oral and peritoneal exposure. It is shown to be nephrotoxic and carcinogenic in male rats, foetotoxic in rats and rabbits, and as teratogenic for rabbit and mouse. It is difficult to use the results obtained in animals to decide toxicity levels in humans. Since, it was observed that toxicity may vary according to the species, or sex in the same species. Toxicity studies on microorganisms and insects could be used, but still the above issues remain debatable (31). Essential oils may be safe at low concentrations, but display toxicity to humans at high concentrations represented as lethal dosages (61). Toxicity in humans has been observed in various situations like exposure to skin, accidental ingestion, exposure to industrial products and clinical trials for cutaneous toxicity. Ingestion of limonene can cause diarrhoea and transient proteinuria in healthy volunteers (31). Few of the well known EOs and their common ingradients have toxic effects on humans at high concentrations. For example, exposure to oils like wormwood oil (*Artemisia absinthium*), *M. pulegium*, calamus oil (*A. calamus*) and mustard oil (*Brassica nigra*) containing thujone, pulegone, -asarone and allyl isocyanate respectively have toxic effects in humans (60). 1,8-Cineole from *E. globulus*, *F. vulgare* containing fenchone, pulegone from *M. pulegium*, *R. officinalis* and its major component camphor, Mentha sp. (with menthol and menthone), *A. absintihium* with thujone are known to exert toxic effects in humans leading to convulsions, hepatic necrosis, dementia, ataxia and hallucinations (31). Some oils were known for their irritant property like Clove oils, *C. sativum* with high linalool content, melissa oii, origanum oil, summer savoury oil, tea tree oil, thyme oil and oil of *Pinus sylvestris*, whereas, some of the EOs like bergamot oil, cumin oil, oil of *Citrus paradisi*, oil of *Citrus limon* and oil of *Citrus sinensis* induce phototoxicity in humans (60). EOs were produce toxic effects during pregnancy and may have abortifacient effects. Also, anise oil (*P. anisum*) and fennel oil (*F. vulgare*) containing anethole, nutmeg oil (*M. fragrans*) containing safrole and myristicin, rosemary oil (*R. officinalis*) with camphor as main constituents should not be used/consumed during pregnancy (60). Calamus oil (*Acorus calamus*) containing -asarone, croton (*Croton tiglium*), basil (*Ocimum* spp), nutmeg (*M. fragrans*) and rose (Rosa spp.) oils containing up to 3.0% of methyl eugenol are reported to be carcinogenic in humans and experimental rodents (40). A recent study demonstrated that the four essential oils – palmarosa, citronella, lemongrass and vetiver induce cytotoxicity and genotoxicity in human lymphocytes at higher concentrations. Also, two terpenoid components of them citral and geraniol exhibit similar effects. However, these oils were found to be safe for human consumption at low concentrations (61). Therefore, it is advisable that EOs should be used very carefully with considerable precautions about the concentrations being used, product application, target consumer, major constituents of the oil and toxicology profile. Since 'the dosage makes the toxin', is very true when we consider the medicinal use of EOs (18).

Essential oils with economic importance in medicinal industry

Nowadays market blooms with the use of plant EOs for perfumery, additives in food/ confectionary as well as for pharmaceuticals and cosmetics. The cosmetics industry uses many herbs and spices in the manufacture of skin creams, balms, shampoos, soaps, and perfumes. Essential oils are also used by soft drink companies and by food companies. Pharmaceuticals, medicinal supplements, and nutriceutical companies are main pillars of industry of hundreds of million dollar based on EOs are increasing consistently in USA, Europe, Africa and in Asian countries (6, 7, 18). The huge production of EOs is achieved mainly by major cultivators and producers like USA, Brazil, India and China. Similarly, Australia, Malaysia, Indonesia, Thailand, Sri Lanka, South Africa, Africa, Egypt, France, Spain, Italy, Germany, Russia, Nepal, Bangladesh and Pakistan are important contributors in worldwide production of EOs. For example, vetiver/khus, clove, lemon grass, basil and celery oils are mainly produced in India. Spain and France are major producers of rosemary obtained from *R. officinalis*. Geranium and rose geranium is obtained from *Pelargonium* sp. which are native of Africa. Tea tree oil from Australia and South Wales, and lavender from Europe areother examples. Approximately 300 EOs are considered important from the commercial point of view (40). EOs which have highest production and market value worldwide can be mentioned as, orange oil, corn mint oil, peppermint oil, eucalyptus oil, citronella oil, lemon oil, clove oil and camphor oil. This is followed by lavender oil, chamomile oil, basil oil, clary sage oil, sage, thyme oil, tarragon oil, wormwood oil, coriander oil, fennel oil, celery oil, anise oil and cumin oils (6). The market value of these oils may vary depending on the source material, purity, composition and many more factors. However, in general, cost of anise oil and coriander oil is calculated around $ 20 to $30 per pound. Comparatively calendula, thyme, dill, summer savoury may cost very high (i.e. more than 6800 Indian currency per pound weight of the oil. Many of these have potential to be used in medicinal industry. EOs obtained from plants are important for medical industry and they belonging to family Apiaceae, Cupressaceae, Lamiaceae, Myrtaceae, Poaceae, Pinaceae, Rutaceae and Taxodiaceae. Anise seed oil (*P. anisum*), caraway (*Carum carvi*), black caraway (*Carum nigrum*), cumin (*C. cyminum*), origano (*O. vulgare*), clove (*S. aromaticum*), tea tree (*M. alternifolia*), coriander (*C. sativum*), sage (*S. officinalis*), summer Savoury (*S. hortensis*), sweet basil (*O. basilicum*), fennel (*F. vulgare*), thyme (*T. vulgaris*), lemon balm (*M. officinalis*), peppermint (*M. piperita*) and german chamomile (*M. chamomilla*) are some of the examples of important EOs (6, 41). Apart from these, few more families like Cupressaceae, Hypericaceae (Clusiaceae), Fabaceae (also known as Leguminosae), Liliaceae, Pinaceae, Piperaceae, Rosaceae, Santalaceae, and Zygophyllaceae are of considerable potential. There is need to explore the EOs from members of these families for various purposes, particularly for medicinal properties (41).

Table 1 – Medicinal properties of some essential oils.

S.N.	Plant family	Essential oil	Medicinal properties
1	Apiaceae (Umbelliferae)	*Carum nigrum* (Black caraway); *Anethum graveolens* (Dill); *Apium graveolens* (Celery); *Foeniculum vulgare* (Fennel); *Pimpinella anisum* (Anise); *Cuminum cyminum* (Cumin); *Corriandrum sativum* (Coriander)	Antibacterial; Antifungal; Anticancer; Antiviral; Anti-diabetic
2	Asteraceae (Compositae)	*Artemisia judaica*; *A. annua*; *A. absinthium* (Wormwood); *A. dracunculus* (Tarragon)	Antifungal; Anticancer; Antiviral
3	Geraniaceae	*Pelargonium graveolens* (Rose Geranium)	Antibacterial
4	Lamiaceae/Labiateae	*Origanum vulgare* (Origano); *Melissa officinalis* (Lemon balm); *Salvia officinalis* (Sage); *Mentha sp.; Mentha longifolia* (Wild Mint); *M. piperita* (Peppermint); *M. spicata* (Spearmint); *Ocimum basilicum* (Sweet Basil); *O. sanctum; Rosmarinus officinalis* (Rosemary); *Lavandula officinalis* (Lavender); *Lavandula sp.*; *Salvia sclarea* (Sage Clary)	Antibacterial; Antifungal; Anticancer; Antiviral; Antidiabetic; Antimutagenic, Antiprotozoal; Anti-inflammatory; Antioxidant
5	Lauraceae	*Cinnamomum* sp. (Cinnamon)	Antimicrobial; Anti-inflammatory; Antimutagenic
6	Liliaceae	*Allium sativum* (Garlic); *Allium cepa* (onion)	Antifungal; Antiviral; Antiprotozoal
7	Myrtaceae	*Syzigium aromaticum* (Clove); *Thymus vulgaris* (Thyme); *Thymus* sp.; *Melaleuca alternifolia* (Tea tree); *Eucalyptus globulus* (Blue gum); *Myristica fragrans* (Nutmeg)	Antibacterial; Antifungal; Anticancer; Antiviral; Antimutagenic Anti-inflammatory Antiprotozoal
8	Oleaceae	*Jasminum* sp.; *Olea europaea* (Olive)	Antibacterial, Anticancer

9	Piperaceae	*Piper nigrum* (Black pepper)	Antibacterial; Antifungal; Anticancer; Antiprotozoal
10	Pinaceae	*Cedrus libani* (Cedar wood oil); *Pinus roxburghii*	Antifungal; Antibacterials
11	Poaceae	*Cymbopogon martini* (Palmarosa); *Cymbopogon citrates* (Lemon grass); *Cymbopogon nardus* (Citronella grass);	Antifungal; Anticancer
12	Rutaceae	*Citrus* sp. (Lemon); *C. paradisi* (Grape fruit)	Antibacterial; Antifungal; Anticancer
13	Rosaceae	Rosa sp.	Antifungal
14	Santalaceae	*Santalum* sp.; *Santalum album* (Sandalwood)	Antiviral
15	Zingiberaceae	*Zingiber officinale* (Ginger); *Zingiber montanum*; *Curcuma longa* (Turmeric); *Elettaria cardamomum* (Cardamom)	Antifungal; Anticancer; Antioxidant; Antimutagenic

Table 2 - Bacteria susceptible to essential oils.

S.N.	Target bacteria	Essential oil	References
1	*Bacillus subtilis*	*Thymus vulgaris* (Thyme); *Thymus* sp.; *Ziziphora clinopodioides* (Blue mint)	(25,26)
2	*Escherichia coli*	*Eucalyptus robusta* (Swamp mahogany); *Thuja occidentalis*; *Pinus roxburghii*; *Juniperus communis*	(13), (10)
3	*Enterobacter aerogenes*; *E. cloacae*	*Origanum vulgare* (Oregano); *Syzigium aromaticum* (Clove)	(13,26)
4	*Enterococcus faecalis*	*Origanum vulgare* (Oregano); *Syzigium aromaticum* (Clove); *Ziziphora clinopodioides* (Blue mint)	(13,19,26)
5	*Haemophilus influenzae*	*Eucalyptus robusta* (Swamp mahogany); *E. saligna*; *E. globulus* (Blue gum); *Salvia sclarea* (Sage Clary).	(15),(16)
6	*Klebsiella pneumoniae*	*Eucalyptus robusta* (Swamp mahogany); *E. saligna*; *E. globulus* (Blue gum); *Salvia sclarea* (Sage Clary); *S. officinalis* (Sage); *S. lavandulifolia*; *S. rosifolia*; *Thymus vulgaris* (Thyme); *Thymus* sp.	(15,16,25)
7	*Mycobacterium avium*	*Melaleuca alternifolia* (Tea tree)	(19)
8	*Mycobacterium tuberculosis*	*Lantana fucata*; *L. trifolia*	(19)
9	*Proteus vulgaris*	*Juglans regia (*Common walnut*); Syzigium aromaticum (*Clove*); Thymus vulgaris (*Thyme*);Thymus* sp.	(14,25)
10	*Pseudomonas aeruginosa*; Drug resistant *P. aeruginosa*	*Carum nigrum (*Black caraway*); Juglans regia (*Common walnut*); Melaleuca alternifolia (*Tea tree*); Syzigium aromaticum (*Clove*); Ziziphora clinopodioides (*Blue mint*); Thymus vulgaris (*Thyme*); Thymus* sp.	(14,19,25,26)
11	*Staphylococcus aureus*	*Apium graveolens* (Celery); *Croton cajucara; Eucalyptus robusta* (Swamp mahogany); *E. saligna*; *E. globulus* (Blue gum); *Juglans regia* (Common walnut); *Ziziphora clinopodioides (*Blue mint*); Thymus vulgaris (*Thyme*); Thymus* sp.; *Salvia sclarea (*Sage Clary*); S. officinalis (*Sage*); S. lavandulifolia; S. rosifolia.*	(14,15,16,19,25,26)
12	*S. epidermidis*	*Juglans regia* (Common walnut); *Ziziphora clinopodioides* (Blue mint)	(25)
13	*Salmonella typhimurium*	*Juglans regia* (Common walnut);	(11, 13 15, 16)

		Melissa officinalis (Lemon balm); *Pinus densiflora* (Japanese red pine); *Pinus koraiensis* (Korean pine); *Rosa* spp.; *Salvia sclarea* (Sage Clary); *S. officinalis* (Sage); *S. lavandulifolia*; *Taxodium distichum*; *Pinus roxburghii*; *Thuja occidentalis*	
14	*Serratia marcescens*	*Myristica fragrans* (Nutmeg); *Origanum vulgare* (Oregano); *Pelargonium graveolens* (Rose Geranium); *Piper nigrum* (Black pepper); *Syzigium aromaticum* (Clove); *Thymus vulgaris* (Thyme); *Thymus* sp.	(14,26)
15	*Streptococcus pneumonia*	*Eucalyptus robusta* (Swamp mahogany); *E. saligna*; *E. globulus* (Blue gum); *Salvia sclarea* (Sage Clary); *S. officinalis* (Sage); *S. lavandulifolia*; *S. rosifolia*; *Thymus vulgaris* (Thyme); *Thymus* sp.	(13,15,16,19,25)
16	*Shigella dyssenteriae*	*Juglans regia* (Common walnut)	(25)
17	*Vibrio cholerae*	*Pinus roxburghii; Taxodium distichum; Thuja occidentalis*	(12)
18	*Yersinia enterocolitica*	*Myristica fragrans* (Nutmeg); *Pelargonium graveolens* (Rose Geranium); *Piper nigrum* (Black pepper); *Syzigium aromaticum* (Clove); *Thymus vulgaris* (Thyme);*Thymus* sp.	(14)

Table 3 – Essential oils active against selected fungal pathogens.

S.N.	Target fungi	Essential oils	References
1	*Alternaria alternata*	*Cedrus libani* (Cedar wood oil); *Cymbopogon martini* (Ginger grass); *C. citrates* (Lemon grass); *Tamarix boveana; Rosmarinus officinalis* (Rosemary); *Foeniculum vulgare* (Fennel)	(9,15,26)
2	*Aspergillus niger*	*Artemisia judaica* (Wormwood); *Cedrus libani* (Cedar wood oil)	(9)
3	*Aspergillus parasiticus*	*Satureja hortensis* (Summer savoury); *Rosmarinus officinalis* (Rosemary)	(15,26)
4	*Aspergillus flavus*	*Cedrus libani* (Cedar wood oil); *Cuminum cyminum* (Cumin); *Nigella sativa* (Black cumin); *Zingiber officinale* (Ginger)	(9,27)
5	*Aspergillus fumigatus*	*Cedrus libani* (Cedar wood oil); *Cuminum cyminum* (Cumin); *Nigella sativa* (Black cumin)	(9,27)
6	*Candida albicans; C. glabrata; Candida* sp.	*Juniperus* spp., *Lavandula* sp.; *Melaleuca alternifolia*; *Piper nigrum* (Black Pepper); *Ziziphora clinopodioides*	(13,19)
7	*Cladosporium cladosporioides*	*Cedrus libani* (Cedar wood oil)	(9)
8	*Cryptococcus neoformans*	*Lavandula* sp.	(27)
9	*Fusarium oxysporum; F. moniliforme; F. solani; F. proliferatum*	*Allium sativum* (Garlic); *Artemisia judaica* (Wormwood); *A. absinthium*; *A. biennis*; other *Artemisia* sp.; *Chenopodium ambrosioides*; *Cymbopogon martini* (Ginger grass); *C. citrates* (Lemon grass); *Tamarix*	(15,26,28,29)

		boveana; *Rosmarinus* (Rosemary); *Zingiber officinale* (Ginger); *Salvia fruticosa*; *S. officinalis*; *S. rosifolia*	
10	*Fonsecaea pedrosoi, Geotrichum candidum, Rhizocotonia solani, Pythium debaryanum*	*Artemisia judaica* (Wormwood); *A. absinthium*; *A. biennis*; other *Artemisia* sp.	(29,30)
11	*Macrophomina phaseolina*	*Chenopodium ambrosioides*	(28)
12	*Microsporum canis; Microsporum gypseum*	*Artemisia judaica* (Wormwood); *A. absinthium*; *A. biennis*; other *Artemisia* sp.; *Cinnamomum* sp; *Croton argyrophylloides*; *C. zehntneri*; *C. cajucara*; *Syzigium aromaticum*; *Daucus carota* (Wild carrot)	(14, 29, 30)
13	*Trichophyton rubrum; T. mentagrophytes; T. roseum*	*Artemisia judaica* (Wormwood); *A. absinthium*; *A. biennis*; *Artemisia* sp.; *Cinnamomum* sp.; Daucus carota (Wild carrot); *Syzigium aromaticum*	(14, 29, 30)

Conclusions and promises

Efforts are being done to further explore the broader range of biological activities of some Gymnospermic essential oils and their significant industrial applications. Novel approaches of chemotherapy and chemoprevention are necessary in the advent of multiple drug resistance related with infectious and non-infectious diseases. There is need to increase the awareness on the risks and benefits associated with the medicinal uses of EOs among the medical and healthcare personnel as well as among the patients using it (31, 33). Use of plant molecules for prophylaxis and treatment of infectious and non-infectious diseases can be a good strategy as it is mostly non-toxic and ecofriendly (9, 10). Antibacterial drugs, antimalarial drug, artemisinin (isolated from *Artemisia annua*) and anticancer drug, taxol (from *Taxus brevifolia*) are popular examples for successful outcome of this approach. Many of the EOs obtained from herbs and spices are commonly used as food ingredients. Certain advantages associated with the use of EOs are less toxicity, reduced genotoxicity, ability to act on multiple cellular targets and low cost of production (9-11). Many of the plant molecules possess an ability to act as chemosensitizers when used in combination and enhance activity of the partner drug. There is need to analyze and document the various components of EOs which possess important medicinal activities. Various analytical techniques have helped phytochemical analysts to reveal the chemical diversity of essential oils and their constituent molecules (9-11). These molecules may act as scaffolds to build novel molecules for therapeutics and offer tremendous scope for further research. In addition, the huge information being generated by in vitro assays need to be confirmed through systematic animal studies and clinical investigations.

Acknowledgements

The authors are thankful to Prof. D. K. Chauhan (HOD) Department of Botany, University of Allahabad, for inspiration and support; to Dr. Rajesh kumar and Dr. Shashi kant Shukla, Rural Technology and Development (RTD) IIDS, University of Allahabad, for their kind support.

References

[1] Press JR, Shrestha KK, Sutton DA. Annotated Checklist of the Flowering Plants of Nepal. The Natural History Museum. 2000.

[2] Wu Z, Raven PH. Flora of China. Vol. 4. Beijing Science Press; 1999.

[3] Gewali MB. Institute of Natural Medicine. Japan: University of Toyama; 2008. Aspects of Traditional Medicine in Nepal; pp. 19–20.

[4] Vallejo MCN, Evandro A, Sergio ALM. Volatile wood oils of the Brazilian *Pinus caribaea* var. *hondurensis* and Spanish *Pinus pinaster* var. *mediterranea*. J Braz Chem Soc. 1994; 5:107–112.

[5] Asta J, Jurgita S, Aida S, Eugenija K. Characteristics of essential oil composition in the needles of young scots pine (*Pinus sylvestris* L.) stands growing along and ariel ammonia gradient. Chemija. 2006; 17:67–73.

[6] Hussain, A.I., Anwar, F., Hussain Sherazi, S.T., Przybylski, R., 2008. Chemical composition, antioxidant and antimicrobial activities of basil (*Ocimum basilicum*) essential oils depends on seasonal variations. Food Chem. 108,986–995.

[7] Teixeira, B., Marques, A., Ramos, C., Neng, N.R., Nogueira, J.M., Saraiva, J.A., Nunes, M.L., 2013. Chemical composition and antibacterial and antioxidant properties of commercial essential oils. Ind.CropsProd.43, 587–595.

[8] Burt, S., 2004. Essential oils: their antibacterial properties and potential applications in foods – a review. Int. J. Food Microbiol. 94, 223–253.

[9] A Dikshit, N.K. Dubey, N.N. Tripathi., S.N. Dikshit, 1983. Cedrus oil – a promising storage fungitoxicant. J. Stored Prod. Res. 19, 159–162.

[10] Ravikant Singh, Ashutosh Pathak, Anupam Dikshit, Rohit K Mishra., ANTIBACTERIAL EVALUATION OF ESSENTIAL OILS OF JUNIPERUS COMMUNIS, PINUS ROXBURGHII AND THUJA OCCIDENTALIS AGAINST ESCHERICHIA COLI. Biochem. Cell. Arch. Vol. 18, No. 1, pp. 241-244, 2018 www.connectjournals.com/bca ISSN 0972-5075.

[11] Ravikant Singh , Ashutosh Pathak, Anupam Dikshit, Rohit Kumar Mishra , "COMPARISION OF BIOLOGICAL ACTIVITIES OF ESSENTIAL OIL OF THREE GYMNOSPERMS AGAINST SALMONELLA TYPHIMURIUM", INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT), ISSN:2320-2882, Volume.6, Issue 1, Page No pp.1420-1426, February 2018, Available at : http://www.ijcrt.org/IJCRT1802181.pdf

[12] Raviaknt Singh, Rinki Singh, Preeti Singh, Saket Jha, Ashutosh Pathak, Shashi Kant Shukla, Anupam Dikshit , Rohit K. Mishra.*"Synergistic Effect of Essential Oils of Three Gymnosperms Against Vibrio Cholerae"*, Volume 6, Issue III, International Journal for Research in Applied Science and Engineering Technology (IJRASET) Page No: , ISSN : 2321-9653, www.ijraset.com

[13] Singh, G., Kapoor, I.P.S., Pandey, S.K., Singh, U.K., Singh, R.K., 2002. Studies on essential oils: part10; antibacterial activity of volatile oils of some spices. Phytother. Res. 16,680–682.

[14] Dorman, H.J.D., Deans, S.G., 2000. Antimicrobial agents from plants: antibacterial activity of plant volatile oils. J. Appl. Microbiol. 88, 308–316.

[15] Rota, C., Carraminana, J.J., Burillo, J., Herrera, A., 2004. In vitro antimicrobial activity of essential oils from aromatic plants against selected food borne pathogens. J. Food Prot. 67, 1252–1256.

[16] Roller, S., Ernest, N., Buckle, J., 2009. The antimicrobial activity of high-necrodane and other lavender oils on methicillin-sensitive and -resistant *Staphylococcus aureus* (MSSA and MRSA). J. Altern. Complement. Med. 15, 275–279.

[17] Djilani, A., Dicko, A., 2012. The therapeutic benefits of essential oils. In: Bouayed, J., Bohn, T. (Eds.), Nutrition, Well-being and Health. InTech, Croatia, pp. 155–178.

[18] Nakatsu, T., Lupo, A.T., Chinn, J.W., Kang, R.K.L., 2000. Biological activity of essential oils and their constituents. Stud. Nat. Prod. Chem. 21, 571–631.

[19] Carson, C.F., Hammer, K.A., Riley, T.V., 2006. Melaleuca alternifolia (Tea Tree) oil: a review of antimicrobial and other medicinal properties. Clin. Microbiol. Rev. 19, 50–62.

[20] Bakkali, F., Averbeck, S., Averbeck, D., Idaomar, M., 2008. Biological effects of essential oils – a review. Food Chem. Toxicol. 46, 446–475.

[21] Samy, R.P., Gopalakrishnakone, P., 2010. Therapeutic potential of plants as antimicrobials for drug discovery. Evid. Based Compl. Altern. Med. 7, 283–294.

[22] Raut, J.S., Karuppayil, S.M., 2014. Bioprospecting of plant essential oils for medicinal uses. In: Fulekar, M.H., Pathak, B., Kale, R.K. (Eds.), Environment and Sustainable Development. Springer, India, pp. 59–76.

[23] Della Loggia R (1993) Pianteofficinali per infusi e tisane. O. E. M. F.: Milan, Italy, pp 283-285.

[24] Leung A Y and Foster S (1996) Encyclopedia of Common Natural Ingredients. Used in food, dugs, and cosmetics. Second Edition; Wiley Interscience: New York, . 325-327.

[25] Rather, M.A., Dar, B.A., Dar, M.Y., Wani, B.A., Shah, W.A., Bhat, B.A., Bashir, A.G., Bhat, K.A., Anand, R., Qurishi, M.A., 2012. Chemical composition, antioxidant and antibacterial activities of the leaf essential oil of *Juglans regia* L. and its constituents. Phytomedicine 19, 1185–1190.

[26] Rosato, A., Vitali, C., De Laurentis, N., Armenise, D., Antonietta, M.M., 2007. Antibacterial effect of some essential oils administered alone or in combination with norfloxacin. Phytomedicine 14, 727–732.

[27] Khosravi, A.R., Minooeianhaghighi, M.H., Shokri, H., 2011. The potential inhibitory effect of *Cuminum cyminum*, *Ziziphora clinopodioides* and *Nigella sativa* essential oils on the growth of Aspergillus fumigatus and Aspergillus flavus. Braz. J. Microbiol. 42, 216–224.

[28] Kumar, R., Mishra, A.K., Dubey, N.K., Tripathi, Y.B., 2007. Evaluation of *Chenopodium ambrosioides* oil as a potential source of antifungal, antiaflatoxigenic and antioxidant activity. Int. J. Food Microbiol. 115, 159–164.

[29] Kordali, S., Kotan, R., Mavi, A., Cakir, A., Ala, A., Yildirim, A., 2005. Determination of the chemical composition and antioxidant activity of the essential oil of *Artemisia dracunculus* and of the antifungal and antibacterial activities of Turkish *Artemisia absinthium*, *A. dracunculus*, *Artemisia santonicum*, and *Artemisia spicigera* essential oils. J. Agric. Food Chem. 53, 9452–9458.

[30] Irkin, R., Korukluoglu, M., 2009. Effectiveness of *Cymbopogon citratus* L. essential oil to inhibit the growth of some filamentous fungi and yeasts. J. Med. Food 12, 193–197.

[31] Vigan, M., 2010. Essential oils: renewal of interest and toxicity. Eur. J. Dermatol. 20, 685–692.

[32] Hammer, K.A., Carson, C.F., Riley, T.V., 1999. Antimicrobial activity of essential oils and other plant extracts. J. Appl. Microbiol. 86, 985–990.

[33] Edris, A.E., 2007. Pharmaceutical and therapeutic potentials of essential oils and their individual volatile constituents: a review. Phytother. Res. 21, 308–323.

[34] Oussalah, M., Caillet, S., Lacroix, M., 2006. Mechanism of action of Spanish oregano, Chinese cinnamon, and savory essential oils against cell membranes and walls of Escherichia coli O157:H7 and Listeria monocytogenes. J. Food. Prot. 69, 1046–1055.

[35] Kathiravan, M.K., Salake, A.B., Chothe, A.S., Dudhe, P.B., Watode, R.P., Mukta, M.S., Gadhwe, S., 2012. The biology and chemistry of antifungal agents: a review. Bioorg. Med. Chem. 20, 5678–5698.

[36] Kumar, A., Shukla, R., Singh, P., Dubey, N.K., 2010. Chemical composition, antifungal and anti-aflatoxigenic activities of Ocimum sanctum L. essential oil and its safety assessment as plant based antimicrobial. Food Chem. Toxicol. 48, 539–543.

[37] Carnesecchi, S., Bras-Goncalves, R., Bradaia, A., Zeisel, M., Gosse, F., Poupon, M.F., Raul, F., 2004. Geraniol, a component of plant essential oils, modulates DNA synthesis and potentiates 5-fluorouracil efficacy on human colon tumor xenografts. Cancer Lett. 215, 53–59.

[38] Tsuneki, H., Ma, E.L., Kobayashi, S., Sekizaki, N., Maekawa, K., Sasaoka, T., Wang, M.W., Kimura, I., 2005. Antiangiogenic activity of eudesmol in-vitro and in-vivo. Eur. J. Pharmacol.512, 105–115.

[39] Vukovic-Gacic, B., Nikcevic, S., Beric-Bjedov, T., Knezevic-Vukcevic, J., Simic, D., 2006. Antimutagenic effect of essential oil of sage (Salvia officinalis L.) and its monoterpenes against UV-induced mutations in Escherichia coli and Saccharomyces cerevisiae. Food Chem.Toxicol.44, 1730–1738.

[40] Bakkali, F., Averbeck, S., Averbeck, D., Idaomar, M., 2008. Biological effects of essential oils – a review. Food Chem. Toxicol. 46, 446–475.

[41] Hammer, K.A., Carson, C.F., 2011. Antibacterial and antifungal activities of essential oils. In: Thormar, H. (Ed.), Lipids and Essential Oils as Antimicrobial Agents. John Wiley & Sons, Ltd, UK, pp. 255–306.

[42] Sauter, I.P., Rossa, G.E., Lucas, A.M., Cibulski, S.P., Roehe, P.M., da Silva, L.A.A., Rott, M.B., Vargas, R.M.F., Cassel, E., von Poser, G.L., 2012. Chemical composition and amoebicidal activity of *Piper hispidinervum* (Piperaceae) essentialoil.Ind.Crops Prod. 40,292–295.

[43] Abdollahi, M., Salehnia, A., Mortazavi, S.H., Ebrahimi, M., Shafiee, A., Fouladian, F., Keshavarz, K., Sorouri, S., Khorasani, R., Kazemi, A., 2003. Antioxidant, antidiabetic, antihyperlipidemic, reproduction stimulatory properties and safety of essential oil of Satureja khuzestanica in ratin vivo: a toxicopharmacological study. Med. Sci. Monit. Int. Med. J. Exp. Clin. Res. 9, BR331-335.

[44] Marles, R.J., Farnsworth, N.R., 1995. Antidiabetic plants and their active constituents. Phytomedicine 2, 137–189.

[45] Misra, B.B., Dey, S., 2013. Evaluation of in vivo anti-hyperglycemic and antioxidant potentials of -santalol and sandalwood oil. Phytomedicine 20, 409–416.

[46] Wajaht, A. S., Qadir, M. Chemical composition, Antioxidant and Antibacterial activity of Thuja orientalis essential oil. World J Pharmaceu. Sci. 2(1): 56-61(2014).

[47] De Flora, S., Bagnasco, M., Vainio, H., 1999. Modulation of genotoxic and related effects by carotenoids and vitamin A in experimental models: mechanistic issues. Mutagenesis 14, 153–172.

[48] Morita, T., Jinno, K., Kawagishi, H., Arimoto, Y., Suganuma, H., Inakuma, T., Sugiyama, K., 2003. Hepatoprotective effect of myristicin from nutmeg (Myristica fragrans) on lipopolysaccharide/d-galactosamine-induced liver injury. J. Agric. Food Chem. 51, 1560–1565.

[49] Mezzoug, N., Elhadri, A., Dallouh, A., Amkiss, S., Skali, N.S., Zhiri, A., Abrini, J., Baudoux, D., Diallo, B., Jaziri, M.E., Idaomar, M., 2007. Investigation of the mutagenic and antimutagenic effects of Origanum compactum essential oil and some of its constituents. Mut. Res. Genet. Toxicol. Environ. Mutagen. 629, 100–110.

[50] Ghaisas, S., Bhide, S., 1994. In vitro studies on chemoprotective effect of purnark against benzopyrene-induced chromosomal damage in human lymphocytes. Cell Biol. Int. 18, 21–28.

[51] Tomaino, A., Cimino, F., Zimbalatti, V., Venuti, V., Sulfaro, V., DePasquale, A., Saija, A., 2005. Influence of heating on antioxidant activity and the chemical composition of some spice essential oils. FoodChem. 89, 549–554.

[52] Mau, J.L., Lai, E.Y., Wang, N.P., Chen, C.C., Chang, C.H., Chyau, C.C., 2003. Composition and antioxidant activity of the essential oil from Curcuma zedoaria. Food Chem. 82, 583–591.

[53] Tepe, B., Donmez, E., Unlu, M., Candan, F., Daferera, D., Vardar-Unlu, G., Polissiou, M., Sokmen, A., 2004. Antimicrobial and antioxidative activities of the essential oils and methanol extracts of Salvia cryptantha (Montbret etAucherexBenth.) and Salvia multicaulis (Vahl). FoodChem.84, 519–525.

[54] Hamid, A.A., Aiyelaagbe, O.O., Usman, L.A., 2011. Essential oils: its medicinal and pharmacological uses. Int. J. Curr. Res. 33, 86–98.

[55] Talpur, N., Echard, B., Ingram, C., Preuss, H., 2005. Effects of an ovel formulation of essential oils on glucose–insulin metabolism in diabetic and hypertensiverats: a pilot study. Diabetes Obesity Metab.7, 193–199.

[56] Saeidnia, S., Gohari, A.R., 2012. Trypanocidal monoterpenes: lead compounds to design future trypanocidal drugs. Stud. Nat. Prod. Chem. 37, 173–189.

[57] Santos, A.O., Santin, A.C., Yamaguchi, M.U., Cortez, L.E.R., Ueda-Nakamura, T., Dias Filho, B.P., Nakamura, C.V., 2010. Antileishmanial activity of an essential oil from the leaves and flowers of Achillea millefolium. Ann. Trop. Med. Parasitol. 104, 475–483.

[58] Tchoumbougnang, F., Zollo, P.H., Dagne, E., Mekonnen, Y., 2005. In vivo anti-malarial activity of essential oils from Cymbopogon citratus and Ocimum gratissimum on mice infected with Plasmodium berghei. Planta Med.71, 20–23.

[59] Armstrong, J.S., 2006. Mitochondrial membrane permeabilization: the sine qua non for cell death. Bioessays 28, 253–260.