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Review

A status review on the medicinal properties of essential oils

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ABSTRACT

Essential oils (EOs) are complex mixtures of low molecular weight compounds extracted from plants by steam distillation and various solvents. Terpenoids and phenylpropanoids are the major constituents which provide characteristic aroma and biological properties to EOs. Essential oils are prescribed for a variety of health problems by traditional systems of medicine, all over the world. Various pharmaceutical and biological activities like, antibacterial, antifungal, anticancer, antimutagenic, antidiabetic, antiviral, antiinflammatory, and antiprotozoal properties are assigned to them. Extensive phytochemical analysis has lead to the characterization and identification of major components of EOs which are of wide interest, especially to cosmetic and pharmaceutical industries. Current status of the bio-active properties of EOs and their medicinal potential are covered in this review.

Contents

1. Introduction

Essential oils of plant origin are one of the important products of agriculture based industry. They are commonly used as flavouring agents in food products, drinks, perfumaries, pharmaceuticals and cosmetics (Burt, 2004; Hussain et al., 2008; Teixeira et al., 2013). Around 3000 essential oils have been produced by using at least 2000 plant species, out of which 300 are important from the commercial point of view. 40,000–60,000 tonnes per annum production with estimated market value of 700 million US $, indicate that production and consumption of essential oils is increasing all over the World (Djilani and Dicko, 2012). Many factors including genetic variation, plant ecotype or variety, plant nutrition, application of fertilizers, geographic location of the plants, surrounding climate, seasonal variations, stress during growth or maturity and also the post harvest drying and storage, affect the chemistry of EOs. In addition, type of plant material used and the method of extraction determine the yield and composition (constituents) of an EO, and thereby decides its characteristic biological properties

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(Croteau, 1986; Alvarez-Castellanos and Pascual-Villalobos, 2003; Hussain et al., 2008). For example, EO from different plant parts like flowers, leaves, stems, roots, fruits and fruit-peels exhibit different biological and medicinal properties. Similarly, solvents of different polarities extract different group of compounds (Cowan, 1999). Many times it is difficult to differentiate and analyze effect of these factors because they influence one another (Terblanche and Kornelius, 2000).

Essential oils are complex mixtures of low molecular weight (usually less than 500 daltons) compounds extracted by steam distillation, hydrodistillation or solvent extraction (Nakatsu et al., 2000). They are usually stored in oil ducts, resin ducts, glands or trichomes (glandular hairs) of the plants (Baser and Demirci, 2007). On commercial scale, steam distillation is a preferred method for the extraction of essential oils (Masango, 2005). EOs may constitute 20–100 different plant secondary metabolites belonging to a variety of chemical classes (Carson and Hammer, 2011). Terpenoids and phenylpropanoids form the major constituents of the essential oils. In addition, few aromatic and aliphatic constituents are also present. Monoterpenes, sesquiterpenes and oxygenated derivatives of these two are the largest group of chemical entities in EOs (Carson et al., 2006). Most of the time the bioactivities of a particular EO is decided by eiether one or two of its main components (Bakkali et al., 2008). But, sometimes overall activity can not be attributed to any of the major constituents and presence of a combination of molecules modify the activity to exert significant effect. For example, it is reported that inhibitory activity of rosemary oil against insect larvae (lepidopteran larvae) is a consequence of synergistic effects of several chemical constituents, while no individual compound show the activity (Isman et al., 2008).

Natural products and their derivaties are important sources of novel therapeutic molecules (Clardy and Walsh, 2004). Plant essential oils possess various applications mainly in health, agriculture, cosmetic and food industries. Use of EOs in traditional systems of medicine is being practiced since ancient times in human history. Researchers from all over the world are trying to characterize a range of biological properties of EOs which includes antimicrobial, antiviral, antimutagenic, anticancer, antioxidant, antiinflammatory, immunomodulatory, and antiprotozoal activities (Bakkali et al., 2008). Efficiencies of various EOs are compared by analyzing the concentrations required to inhibit the growth of target organisms. Generally, minimum growth inhibitory concentrations (MICs), minimum lethal concentrations (MBCs or MFCs), MIC_{50} and LD_{50} values are used for comparison of bioactivities. These values are obtained with standardized methodologies. For example, protocols given by Clinical Laboratory Standards Institute (CLSI) and cell viability assessment by MTT or XTT assays are used for antimicrobial susceptibility testing (Bakkali et al., 2008; Hammer and Carson, 2011; Schnitzler et al., 2011).

Emergence of drug resistant strains of pathogens, increase in the immunocompromised population and limitations of the available antibiotics/drugs have motivated people to use the complementary and alternative therapies, including the use of EOs. Secondary metabolites which are naturally synthesized by plants in response to attack by insect pest and some times herbivores, constitute a complex mixture of EOs. These small molecule metabolites alone and in combination, (for example in the form of EOs) possess significant medicinal properties; hence, may be used for chemotherapy of infectious as well as non-infectious diseases (Samy and Gopalakrishnakone, 2010; Raut and Karuppayil, 2014).

2. Taxanomy of essential oil producing plants

Plants producing EOs belong to various genera distributed to around 60 families. Selected families such as Alliaceae, Apiaceae, Asteraceae, Lamiaceae, Myrtaceae, Poaceae and Rutaceae are well known for their ability to produce EOs of medicinal and industrial value (Table 1) (Vigan, 2010; Hammer and Carson, 2011). All of the EO producing plant families are rich in terpenoids. While, plant families like Apiaceae (Umbelliferae), Lamiaceae, Myrtaceae, Piperaceae and Rutaceae contain phenylpropanoids more frequently (Chami et al., 2004). Plants from these families are used for EO production at commercial level. For example, coriander, anise, dill and fennel oils are extracted from the plants – *Coriandrum sativum*, *Pimpinella anisum*, *Anethum graveolens* and *Foeniculum vulgare*, respectively. All of these belong to the family Apiaceae

Table 1
Essential oils of medicinal importance distributed to selected plant families.

Sr. no.	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)	Antifungal
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

and are well known for their antibacterial, antifungal, anticancer and antiviral activities. Also, many genera which are well-known for chemotherapeutic, antiviral, antimicrobial, antimutagenic, antioxidant and anti-inflammatory properties belong to the Lamiaceae family. These are also useful against intestinal disorders and bronchitis. *Mentha piperita*, *Rosmarinus officinalis*, *Ocimum basilicum*, *Salvia officinalis*, *Origanum vulgare*, *Melissa officinalis, Satureja hortensis, Thymus vulgaris* and *Lavandula angustifolia* are some of the popular examples of EO producing plants from Lamiaceae (Burt, 2004; Hammer et al., 2006; Hussain et al., 2008). Cinnamon oil which is rich in eugenol, obtained from *Cinnamomum verum*, is an important example from Lauraceae family. It displays antimicrobial and anticancer potential. Many commercially important plants belong to the family Myrtaceae. For example, *Melaleuca alternifolia*, *Eucalyptus globulus*, *Syzygium aromaticum* (*Eugenia caryophyllus*) and *Myrtus communis* produce EOs with well known antibacterial, antifungal, antitumor, anticancer and antiviral properties (Burt, 2004; Hammer et al., 2006).

The family of grasses, Poaceae family includes producer of lemongrass oil (from *Cymbopogon citratus*), citronella oil (from *C. nardus*) and palmarosa (*C. martinii*) oils. The medicinally active components of these EOs like citral, geraniol and geranyl acetate show antimicrobial and anticancer properties. Citrus oils which constitute limonene and linalool are derived from the fruit peel of plants which belong to the Rutaceae family. These components exhibit antimicrobial potential. The plants *Pelargonium graveolens* and *Santalum* spp. of the family Geraniaceae and Santalaceae, respectively possess two important oils *i.e.* geranium and sandalwood oil (Hussain et al., 2008; Bedi et al., 2010). Few more families like Cupressaceae, Hypericaceae (Clusiaceae), Fabaceae (also known as Leguminosae), Liliaceae, Pinaceae and Zygophyllaceae may produce EOs with significant biological activities, which need to be explored (Hammer and Carson, 2011).

3. Essential oils as antibacterial agents

Severity of bacterial infections has gone up even after the discovery of many antibiotics, mainly due to emergence of antibiotic resistant strains, increase in the population with lowered immunity and increased incidences of drug resistant biofilm associated infections. Therefore, infectious diseases caused by bacteria are still one of the leading causes of deaths (Ahmad and Beg, 2001; Hall-Stoodley et al., 2004). In addition, toxicity due to side effects limits the prolonged use of high concentrations of available antibacterial drugs. As such there is a need to explore novel molecules and alternative approaches against pathogenic bacteria (Galvao et al., 2012). Plant molecules are wellknown for their antimicrobial properties. Especially plant EOs have been shown to exhibit broad spectrum inhibitory activities against various Gram positive and Gram negative bacterial pathogens (Table 2) (Edris, 2007; Lang and Buchbauer, 2012; Teixeira et al., 2013). The antibacterial efficacy may vary with oils as well as with different bacteria. For example, sandalwood (*Santalum album*), manuka oil (*Leptospermum scoparium*) and vetiver (*C. zizanioides*) oils, are highly active against Gram positive bacteria, but do not have activity against Gram negative (Hammer et al., 1999; Hammer and Carson, 2011). Compared to other bacteria *Pseudomonas aeruginosa* exhibit tolerance to inhibition by plant EOs. In general, thyme, oregano, tea-tree, cinnamon, lemon grass, bay, lemon-myrtle, clove and rosewood oils are the most active antimicrobials. They are active at concentrations < 1% vol/vol *i.e.* exhibit MICs of < 1% (Hammer et al., 1999; Oussalah et al., 2006). Bay, clove, lemon grass, oregano and thyme inhibit growth of *Escherichia coli* at concentrations of 0.02, 0.04, 0.06, 0.05 and 0.05%, respectively. Thyme, rosemary peppermint, lemon grass, clove and bay oils have potential to prevent *Staphylococcus aureus* at concentrations of $\leq$ 0.05%, while basil and eucalyptus oils inhibit it at 1% concentration (Smith-Palmer et al., 1998; Hammer et al., 1999; Hammer and Carson, 2011). Interestingly, garlic, lemon myrtle and tea-tree oils are very active against methicillin resistant *Staphylococcus aureus* (MRSA) (Tsao and Yin, 2001; Hayes and Markovic, 2003). 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 (Carson et al., 2006; Lambert et al., 2001; Ultee et al., 2002).

Many of the plant molecules are effective against drug sensitive as well as drug resistant strains (May et al., 2000; Bozin et al., 2006). Interestingly, oils of plant origin are shown to possess potential against biofilms which are well tolerant to bacterial antibiotics (Galvao et al., 2012). 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 (Edris, 2007; Saad et al., 2013). Similarly, interference in proton pump activity, loss of membrane integrity, leakage of cellular contents can result in loss of viability (Oussalah et al., 2006; Di Pasqua et al., 2007). Other important mechanisms of action include, denaturation of cytoplasmic proteins and inactivation of cellular enzymes leading to bacterial cell death (Gustafson et al., 1998; Burt, 2004).

4. Antifungal activities of essential oils

Being eukaryotes, pathogenic fungi have similarities with their hosts, both at cellular and molecular levels. Hence, fungi are hard target to hit at (Routh et al., 2011). Some of the opportunistic fungal pathogens (for example, *Candida* spp., *Aspergillus* spp., *Cryptococcus* sp.) are notorious and trouble a large population of immunocompromised patients. There are limited options of drugs available for successful antifungal chemotherapy (Kathiravan et al., 2012). Oncome of drug resistant strains, device associated biofilm infections and side effects of currently prescribed drugs pose difficulties for prevention and treatment of fungal infections. Therefore, invasive fungal infections are associated with very high morbidity and mortality rates (Sardi et al., 2013). Various, plant and human pathogenic fungi, including yeasts are found to be susceptible to EOs (Table 3). The efficiency of inhibition varies with the target organisms and the oil tested. For example, three members of apiaceae family show variable anti *Candida albicans* activity with a trend of coriander > anise > fennel; with the MICs of 0.25%, 0.5% and 1%, respectively (Hammer et al., 1999). Generally *Cymbopogon* sp. shows promising activities against pathogenic yeast (Irkin and Korukluoglu, 2009). Among different EOs, cinnamon, lemongrass, Japanese mint, ginger grass, geranium and clove oils were observed as most promising against *C. albicans*. The effective concentrations range from 0.01 to 0.15% (Devkatte et al., 2005; Hammer and Carson, 2011). Growth of dermatophytes and their spore development is inhibited readily with EOs rich in phenylpropanoids like eugenol and the monocyclic sesquiterpene alcohols such as α-bisabolol (Bajpai et al., 2009; Maxia et al., 2009; Pragadheesh et al., 2013). Growth and aflatoxin production in moulds like *Aspergillus flavus* is prevented by EOs of plant origin (Kumar et al., 2010; Lang and Buchbauer, 2012). 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*

Table 2
Bacteria susceptible to essential oils.

Sr. no.	Target bacteria	Essential oil	References
1	*Aeromonas hydrophila*	*Origanum vulgare* (Oregano); *Pelargonium graveolens* (Rose Geranium); *Piper nigrum* (Black pepper); *Syzigium aromaticum* (Clove); *Thymus vulgaris* (Thyme); *Thymus* sp.	Dorman and Deans (2000), Tepe et al. (2004), Lopez et al. (2005, 2007), Bozin et al. (2006), Rosato et al. (2007)
2	*Alcaligenes faecalis*	*Origanum vulgare* (Oregano); *Pelargonium graveolens* (Rose Geranium); *Piper nigrum* (Black pepper); *Syzigium aromaticum* (Clove); *Thymus vulgaris* (Thyme); *Thymus* sp.	Dorman and Deans (2000), Tepe et al. (2004), Lopez et al. (2005, 2007), Bozin et al. (2006), Rosato et al. (2007)
3	*Bacillus cereus*	*Carum nigrum* (Black caraway); *Santolina rosmarinifolia* (Cotton Lavender)	Singh et al. (2006), Ioannou et al. (2007)
4	*Bacillus subtilis*	*Juglans regia* (Common walnut); *Melissa officinalis* (Lemon balm); *Myristica fragrans* (Nutmeg); *Origanum vulgare* (Oregano); *Pelargonium graveolens* (Rose Geranium); *Piper nigrum* (Black pepper); *Rosa* sp.; *Syzigium aromaticum* (Clove); *Ziziphora clinopodioides* (Blue mint); *Thymus vulgaris* (Thyme); *Thymus* sp.	Dorman and Deans (2000), Mimica-Dukic et al. (2004), Tepe et al. (2004), Lopez et al. (2005, 2007), Bozin et al. (2006), Sonboli et al. (2006), Rosato et al. (2007), Hirulkar and Agrawal (2010), Rather et al. (2012)
5	*Escherichia coli*	*Anethum graveolens* (Dill); *Apium graveolens* (Celery); *Eucalyptus robusta* (Swamp mahogany); *E. saligna; E. globulus* (Blue gum); *Juglans regia* (Common walnut); *Melaleuca alternifolia* (Tea tree); *Melissa officinalis* (Lemon balm); *Mentha longifolia* (Wild Mint); *M. piperita* (Peppermint); *M. spicata* (Spearmint); *Pimpinella anisum* (Aniseed); *Myristica fragrans* (Nutmeg); *Origanum vulgare*(Oregano); *Pelargonium graveolens* (Rose Geranium); *Pinus densiflora* (Japanese red pine); *Pinus koraiensis* (Korean pine); *Piper nigrum* (Black pepper); *Rosa* spp.; *Salvia sclarea* (Sage Clary); *S. officinalis* (Sage); *S. lavandulifolia*; *S. rosifolia*; *Santolina rosmarinifolia* (Cotton Lavender); *Syzigium aromaticum* (Clove); *Tamarix boveana* (Salt cedar); *Ziziphora clinopodioides* (Blue mint); *Thymus vulgaris* (Thyme); *Thymus* sp.	Dorman and Deans (2000), Delaquis et al. (2002), Singh et al. (2002), Dryden et al. (2004), Hong et al. (2004), Mimica-Dukic et al. (2004), Rota et al. (2004), Tepe et al. (2004), Bozin et al. (2006), Carson et al. (2006), Sonboli et al. (2006), Fabio et al. (2007), Lopez et al. (2005, 2007), Ioannou et al. (2007), Rafii and Shahverdi (2007), Rosato et al. (2007), Sartorelli et al. (2007), Saidana et al. (2008), Roller et al. (2009), Hirulkar and Agrawal (2010), Baananou et al. (2012), Djenane et al. (2012), Galvao et al. (2012), Rather et al. (2012)
6	*Enterobacter aerogenes*; *E. cloacae*	*Mentha longifolia* (Wild Mint); *M. piperita* (Peppermint); *M. spicata* (Spearmint); *Origanum vulgare* (Oregano); *Pelargonium graveolens* (Rose Geranium); *Piper nigrum* (Black pepper); *Rosa* spp.; *Syzigium aromaticum* (Clove)	Dorman and Deans (2000), Singh et al. (2002), Tepe et al. (2004), Lopez et al. (2005), Bozin et al. (2006, 2007), Fabio et al. (2007), Rafii and Shahverdi (2007), Rosato et al. (2007), Hirulkar and Agrawal (2010), Djenane et al. (2012)
7	*Enterococcus faecalis*	*Melaleuca alternifolia* (Tea tree); *Origanum vulgare* (Oregano); *Pelargonium graveolens* (Rose Geranium); *Piper nigrum* (Black pepper); *Syzigium aromaticum* (Clove); *Ziziphora clinopodioides* (Blue mint); *Thymus vulgaris* (Thyme); *Thymus* sp.	Dorman and Deans (2000), Singh et al. (2002), Dryden et al. (2004), Tepe et al. (2004), Lopez et al. (2005, 2007), Bozin et al. (2006, 2007), Carson et al. (2006), Sonboli et al. (2006), Fabio et al. (2007), Rosato et al. (2007), Shan et al. (2007)
8	*Haemophilus influenzae*	*Eucalyptus robusta* (Swamp mahogany); *E. saligna; E. globulus* (Blue gum); *Eugenia caryophyllus* (Clove); *Melaleuca alternifolia* (Tea tree); *Mentha longifolia* (Wild Mint); *M. piperita* (Peppermint); *M. spicata* (Spearmint); *Salvia sclarea* (Sage Clary); *S. officinalis* (Sage); *S. lavandulifolia; S. rosifolia*	Rota et al. (2004), Carson et al. (2006), Fabio et al. (2007), Sartorelli et al. (2007), Shan et al. (2007), Rafii and Shahverdi (2007), Roller et al. (2009), Djenane et al. (2012), Galvao et al. (2012)
9	*Klebsiella pneumoniae*	*Anethum graveolens* (Dill); *Eucalyptus robusta* (Swamp mahogany); *E. saligna; E. globulus* (Blue gum); *Eugenia caryophyllus* (Clove); *Juglans regia* (Common walnut), *Mentha longifolia* (Wild Mint); *M. piperita* (Peppermint); *M. spicata* (Spearmint); *Myristica fragrans* (Nutmeg); *Origanum vulgare* (Oregano); *Pelargonium graveolens* (Rose Geranium); *Pinus densiflora* (Japanese red pine); *Pinus koraiensis* (Korean pine); *Piper nigrum* (Black pepper); *Rosa* spp.; *Salvia sclarea* (Sage Clary); *S. officinalis* (Sage); *S. lavandulifolia;S. rosifolia*; *Syzigium aromaticum* (Clove); *Ziziphora clinopodioides* (Blue mint); *Thymus vulgaris* (Thyme); *Thymus* sp.	Dorman and Deans (2000), Delaquis et al. (2002), Hong et al. (2004), Rota et al. (2004), Tepe et al. (2004), Bozin et al. (2006), Carson et al. (2006), Sonboli et al. (2006), Fabio et al. (2007), Lopez et al. (2005, 2007), Rafii and Shahverdi (2007), Rosato et al. (2007), Shan et al. (2007), Roller et al. (2009), Hirulkar and Agrawal (2010), Djenane et al. (2012), Galvao et al. (2012), Rather et al. (2012)
10	*Mycobacterium avium*	*Melaleuca alternifolia* (Tea tree)	Dryden et al. (2004), Carson et al. (2006)
11	*Mycobacterium tuberculosis*	*Lantana fucata; L. trifolia*	Juliao et al. (2009)
12	*Proteus vulgaris*	*Juglans regia* (Common walnut); *Myristica fragrans* (Nutmeg); *Pelargonium graveolens* (Rose Geranium); *Rosa* sp.; *Syzigium aromaticum* (Clove); *Thymus vulgaris* (Thyme);*Thymus* sp.	Dorman and Deans (2000), Hirulkar and Agrawal (2010), Rather et al. (2012)
13	*Pseudomonas aeruginosa*; Drug resistant *P. aeruginosa*	*Apium graveolens* (Celery); *Carum nigrum* (Black caraway); *Juglans regia* (Common walnut); *Melaleuca alternifolia* (Tea tree); *Origanum vulgare* (Oregano); *Pelargonium graveolens* (Rose Geranium); *Piper nigrum* (Black pepper); *Rosa* spp.; *Syzigium aromaticum* (Clove); *Tamarix boveana* (Salt cedar); *Ziziphora clinopodioides* (Blue mint); *Thymus vulgaris* (Thyme); *Thymus* sp.	Dorman and Deans (2000), Singh et al. (2006), Dryden et al. (2004), Tepe et al. (2004), Bozin et al. (2006), Carson et al. (2006), Sonboli et al. (2006), Lopez et al. (2005, 2007), Rosato et al. (2007), Saidana et al. (2008), Hirulkar and Agrawal (2010), Baananou et al. (2012), Rather et al. (2012)

Table 2 (*Continued*)

Sr. no.	Target bacteria	Essential oil	References
14	*Staphylococcus aureus*; Methicillin Resistant *Staphylococcus aureus* (MRSA)	*Apium graveolens* (Celery); *Croton cajucara; Eucalyptus robusta* (Swamp mahogany); *E. saligna; E. globulus* (Blue gum); *Eugenia caryophyllus* (Clove); *Juglans regia* (Common walnut); *Lavandula angustifolia* (Common Lavender); *L. latifolia; L. luisieri; Melaleuca alternifolia* (Tea tree); *Melissa officinalis* (Lemon balm); *Mentha longifolia* (Wild Mint); *M. piperita* (Peppermint); *M. spicata* (Spearmint); *Myristica fragrans* (Nutmeg); *Origanum vulgare* (Oregano); *Pelargonium graveolens* (Rose Geranium); *Pinus densiflora* (Japanese red pine); *Pinus koraiensis* (Korean pine); *Piper nigrum* (Black pepper); *Rosa* spp.; *Rosmarinus officinalis* (Rosemary); *Salvia sclarea* (Sage Clary); *S. officinalis* (Sage); *S. lavandulifolia*; *S. rosifolia*; *Santolina rosmarinifolia* (Cotton Lavender); *Skimmia laureola*; *Syzigium aromaticum* (Clove); *Tamarix boveana* (Salt cedar); *Ziziphora clinopodioides* (Blue mint); *Thymus vulgaris* (Thyme); *Thymus* sp.	Dorman and Deans (2000), Delaquis et al. (2002), Dryden et al. (2004), Mimica-Dukic et al. (2004), Rota et al. (2004), Tepe et al. (2004), Alviano et al. (2005), Bozin et al. (2006), Carson et al. (2006), Sonboli et al. (2006), Fabio et al. (2007), Lopez et al. (2005, 2007), Ioannou et al. (2007), Rafii and Shahverdi (2007), Rosato et al. (2007), Sartorelli et al. (2007), Shan et al. (2007), Saidana et al. (2008), Roller et al. (2009), Hirulkar and Agrawal (2010), Tohidpour et al. (2010), Baananou et al. (2012), Djenane et al. (2012), Galvao et al. (2012), Rather et al. (2012), Shah et al. (2012)
15	*S. epidermidis*	*Juglans regia* (Common walnut); *Skimmia laureola*; *Tamarix boveana* (Salt cedar); *Ziziphora clinopodioides* (Blue mint)	Sonboli et al. (2006), Saidana et al. (2008), Rather et al. (2012), Shah et al. (2012)
16	Streptococcus pneumonia; S. pyogenes; S. agalactiae; *S. haemolyticus*	*Eucalyptus robusta* (Swamp mahogany); *E. saligna; E. globulus* (Blue gum); *Eugenia caryophyllus* (Clove); *Melaleuca alternifolia* (Tea tree); *Mentha longifolia* (Wild Mint); *M. piperita* (Peppermint); *M. spicata* (Spearmint); *Rosa* spp.; *Salvia sclarea* (Sage Clary); *S. officinalis* (Sage); *S. lavandulifolia*; *S. rosifolia*; *Thymus vulgaris* (Thyme); *Thymus* sp.; *Coriandrum sativum* (Coriander)	Delaquis et al. (2002), Singh et al. (2002), Dryden et al. (2004), Lo Cantore et al. (2004), Rota et al. (2004), Carson et al. (2006), Fabio et al. (2007), Rafii and Shahverdi (2007), Sartorelli et al. (2007), Shan et al. (2007), Roller et al. (2009), Hirulkar and Agrawal (2010), Djenane et al. (2012), Galvao et al. (2012), Rather et al. (2012), Shah et al. (2012)
17	*Salmonella typhimurium*	*Coriandrum sativum* (Coriander); *Juglans regia* (Common walnut); *Melissa officinalis* (Lemon balm); *Pinus densiflora* (Japanese red pine); *Pinus koraiensis* (Korean pine); *Rosa* spp.; *Salvia sclarea* (Sage Clary); *S. officinalis* (Sage); *S. lavandulifolia*; *S. rosifolia*; *Tamarix boveana* (Salt cedar)	Delaquis et al. (2002), Singh et al. (2002), Hong et al. (2004), Lo Cantore et al. (2004), Mimica-Dukic et al. (2004), Rota et al. (2004), Fabio et al. (2007), Roller et al. (2009), Hirulkar and Agrawal (2010), Saidana et al. (2008)
18	*Serratia marcescens*	*Myristica fragrans* (Nutmeg); *Origanum vulgare* (Oregano); *Pelargonium graveolens* (Rose Geranium); *Piper nigrum* (Black pepper); *Syzigium aromaticum* (Clove); *Thymus vulgaris* (Thyme); *Thymus* sp.	Dorman and Deans (2000), Tepe et al. (2004), Lopez et al. (2005, 2007), Bozin et al. (2006), Rosato et al. (2007)
19	*Shigella dyssenteriae;*	*Juglans regia* (Common walnut); *Ocimum basilicum* (Sweet Basil); *O. gratissimucum* (African Basil)	Iwalokun et al. (2003), Bozin et al. (2006), Rather et al. (2012)
20	*Listeria monocytogenes*	*Coriandrum sativum* (Coriander); *Pinus densiflora* (Japanese red pine); *Pinus koraiensis* (Korean pine)	Delaquis et al. (2002), Singh et al. (2002), Hong et al. (2004), Lo Cantore et al. (2004)
21	*Micrococcus luteus*	*Myristica fragrans* (Nutmeg); *Pelargonium graveolens* (Rose Geranium); *Piper nigrum* (Black pepper); *Syzigium aromaticum* (Clove); *Tamarix boveana* (Salt cedar); *Thymus vulgaris* (Thyme); *Thymus* sp.	Dorman and Deans (2000), Saidana et al. (2008)
20	*Moraxella* sp.	*Myristica fragrans* (Nutmeg); *Origanum vulgare* (Oregano); *Pelargonium graveolens* (Rose Geranium); *Piper nigrum* (Black pepper); *Syzigium aromaticum* (Clove); *Thymus vulgaris* (Thyme); *Thymus* sp.	Dorman and Deans (2000), Tepe et al. (2004), Lopez et al. (2005, 2007), Bozin et al. (2006), Rosato et al. (2007)
21	*Yersinia enterocolitica*	*Myristica fragrans* (Nutmeg); *Pelargonium graveolens* (Rose Geranium); *Piper nigrum* (Black pepper); *Syzigium aromaticum* (Clove); *Thymus vulgaris* (Thyme);*Thymus* sp.	Dorman and Deans (2000)

Table 3
Essential oils active against selected fungal pathogens.

Sr. no.	Target fungi	Essential oil	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)	Dikshit et al. (1983), Mimica-Dukic et al. (2004), Rota et al. (2004), Ozcan and Chalchat (2008), Rosato et al. (2007), Rasooli et al. (2008), Saidana et al. (2008), Peighami-Ashnaei et al. (2008)
2	*Aspergillus niger*	*Allium sativum* (Garlic); *Artemisia judaica* (Wormwood); *A. absinthium; A. biennis; Carum nigrum* (Black caraway); *Cedrus libani* (Cedar wood oil); *Chenopodium ambrosioides*; *Cymbopogon martini* (Ginger grass); *C. citrates* (Lemon grass); *Eugenia caryophyllus* (Clove); *Foeniculum vulgare* (Fennel); *Juniperi aetheroleum* (Juniper); *Matricaria chamomilla* (Chamomile); *Zingiber officinale* (Ginger); *Tamarix boveana*	Dikshit et al. (1983), Saikia et al. (2001), Benkeblia (2004), Mimica-Dukic et al. (2004), Kordali et al. (2005), Pepeljnjak et al. (2005), Kumar et al. (2007), Agarwal et al. (2008), Bansod and Rai (2008), Lopes-Lutz et al. (2008), Saidana et al. (2008), Singh et al. (2008), Cetin et al. (2009), Irkin and Korukluoglu (2009), Peighami-Ashnaei et al. (2008), Tolouee et al. (2010)
3	*Aspergillus parasiticus*	*Satureja hortensis* (Summer savoury); *Rosmarinus officinalis* (Rosemary)	Rota et al. (2004), Rosato et al. (2007), Ozcan and Chalchat (2008), Rasooli et al. (2008), Razzaghi-Abyaneh et al. (2008)
4	*Aspergillus flavus*	*Carum nigrum* (Black caraway); *Cedrus libani* (Cedar wood oil); *Cuminum cyminum* (Cumin); *Nigella sativa* (Black cumin); *Zingiber officinale* (Ginger); *Satureja hortensis* (Summer savoury)	Dikshit et al. (1983), Singh et al. (2006), Singh et al. (2010), Razzaghi-Abyaneh et al. (2008), Khosravi et al. (2011)
5	*Aspergillus fumigatus*	*Cedrus libani* (Cedar wood oil); *Chenopodium ambrosioides*; *Cuminum cyminum* (Cumin); *Eugenia caryophyllus* (Clove); *Nigella sativa* (Black cumin)	Dikshit et al. (1983), Kumar et al. (2007), Bansod and Rai (2008), Khosravi et al. (2011)
6	*Botrytis cinerea*; *Botrytis fabae*	*Rosmarinus officinalis* (Rosemary); *Foeniculum vulgare* (Fennel); *Artemisia judaica* (Wormwood); *A. absinthium*; *A. biennis*; other *Artemisia* sp.	Mimica-Dukic et al. (2004), Rota et al. (2004), Kordali et al. (2005), Rosato et al. (2007), Ozcan and Chalchat (2008), Lopes-Lutz et al. (2008), Rasooli et al. (2008), Cetin et al. (2009), Irkin and Korukluoglu (2009), Peighami-Ashnaei et al. (2008)
7	*Candida albicans*; *C. glabrata*; *Candida* sp.	*Cinnamomum* sp.; *Croton cajucara*; *Cymbopogon martini* (Ginger grass); *C. citrates* (Lemon grass); *Eucalyptus saligna* (Saligna); *Eugenia caryophyllus* (Clove); *Juniperi aetherole* (Juniper); *Lavandula* sp.; *Melaleuca alternifolia*; *Melissa officinalis*; *Mentha piperita; M. longifolia; M. viridis*; *Ocimum* sp.; *Ocimum sanctum* (Holy Basil/Tulsi); *Pimpinella anisum*; *Piper nigrum* (Black Pepper); *Ziziphora clinopodioides*; *Santolina rosmarinifolia*	Mastura et al. (1999), Saikia et al. (2001), Singh et al. (2002), Dryden et al. (2004), Mimica-Dukic et al. (2004), Alviano et al. (2005), Devkatte et al. (2005), Pepeljnjak et al. (2005), Carson et al. (2006), Ioannou et al. (2007), Sartorelli et al. (2007), Agarwal et al. (2008), Bansod and Rai (2008), Irkin and Korukluoglu (2009), Mkaddem et al. (2009), Khosravi et al. (2011), Zore et al. (2011b); Zuzarte et al. (2011, 2012), Rabadia et al. (2012)
8	*Cladosporium cladosporioides; C. herbarum*	*Cedrus libani* (Cedar wood oil); *Artemisia judaica* (Wormwood); *A. absinthium; A. biennis; Artemisia* sp.	Dikshit et al. (1983), Kordali et al. (2005), Lopes-Lutz et al. (2008), Cetin et al. (2009), Irkin and Korukluoglu (2009)
9	*Cryptococcus neoformans*	*Lavandula* sp.; *Ziziphora clinopodioides*	Khosravi et al. (2011), Zuzarte et al. (2011, 2012)
10	*Penicillium cyclopium*; *P. purpurogenum; P. madriti; P. viridicatum*; *P. roquefortii; Penicillium* sp.	*Allium sativum* (Garlic); *Artemisia judaica* (Wormwood); *A. absinthium; A. biennis;* other *Artemisia* sp.; *Tamarix boveana*; *Carum nigrum* (Black caraway); *Cymbopogon martini* (Ginger grass); *C. citrates* (Lemon grass)	Saikia et al. (2001), Benkeblia (2004), Kordali et al. (2005), Singh et al. (2006), Agarwal et al. (2008), Lopes-Lutz et al. (2008), Saidana et al. (2008), Cetin et al. (2009), Irkin and Korukluoglu (2009)
11	*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 boveana*; *Rosmarinus officinalis* (Rosemary); *Zingiber officinale* (Ginger); *Salvia fruticosa; S. officinalis; S. rosifolia*	Saikia et al. (2001), Benkeblia (2004), Rota et al. (2004), Kordali et al. (2005), Fabio et al. (2007), Kumar et al. (2007), Rosato et al. (2007), Agarwal et al. (2008), Lopes-Lutz et al. (2008), Ozcan and Chalchat (2008), Rasooli et al. (2008), Saidana et al. (2008), Singh et al. (2008), Cetin et al. (2009), Irkin and Korukluoglu (2009), Ozek et al. (2010)
12	*Fonsecaea pedrosoi*	*Artemisia judaica* (Wormwood); *A. absinthium; A. biennis; other Artemisia* sp.	Kordali et al. (2005), Lopes-Lutz et al. (2008), Cetin et al. (2009), Irkin and Korukluoglu (2009)
13	*Geotrichum candidum*	*Artemisia judaica* (Wormwood); *A. absinthium; A. biennis; other Artemisia* sp.	Kordali et al. (2005), Lopes-Lutz et al. (2008), Cetin et al. (2009), Irkin and Korukluoglu (2009)
14	*Rhizocotonia solani*	*Artemisia judaica* (Wormwood); *A. absinthium; A. biennis; other Artemisia* sp.	Kordali et al. (2005), Lopes-Lutz et al. (2008), Cetin et al. (2009), Irkin and Korukluoglu (2009)
15	*Macrophomina phaseolina*	*Chenopodium ambrosioides*	Kumar et al. (2007)
16	*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)	Mastura et al. (1999), Dorman and Deans (2000), Alviano et al. (2005), Kordali et al. (2005), Fontenelle et al. (2008), Lopes-Lutz et al. (2008), Tavares et al. (2008), Cetin et al. (2009), Irkin and Korukluoglu (2009), Pinto et al. (2009)
17	*Mucor ramannianus*	*Mentha piperita; M. longifolia; M. viridis*	Agarwal et al. (2008), Mkaddem et al. (2009)
18	*Pythium debaryanum*	*Artemisia judaica* (Wormwood); *A. absinthium; A. biennis; other Artemisia* sp.	Kordali et al. (2005), Lopes-Lutz et al. (2008), Cetin et al. (2009), Irkin and Korukluoglu (2009)
19	*Trichophyton rubrum; T. mentagrophytes*; *T. roseum*	*Artemisia judaica* (Wormwood); *A. absinthium; A. biennis; Artemisia* sp.; *Cinnamomum* sp.; *Daucus carota* (Wild carrot); *Syzigium aromaticum*	Mastura et al. (1999), Dorman and Deans (2000), Kordali et al. (2005), Lopes-Lutz et al. (2008), Cetin et al. (2009), Irkin and Korukluoglu (2009), Pinto et al. (2009)

niger, *A. flavus*, *Penicillium verrucosum* and *P. chrysogenum* at <1% of concentration (Viuda-Martos et al., 2008).

Drug sensitive as well as resistant pathogenic yeasts, including the major pathogen of humans, *C. albicans*, were inhibited by terpenoid rich EOs (Devkatte et al., 2005; Zore et al., 2011b). Efficacy of essential oils and their components against drug resistant biofilms of *C. albicans* is of importance. These activities may be mediated through inhibition of membrane ergosterol and signalling pathways involved in yeast to hyphae morphogenesis (Agarwal et al., 2008; Raut et al., 2013b, 2013c). 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 (Zore et al., 2011a). Similarly eugenol, thymol and carvacrol affect Ca^{2+} and H^{+} homeostasis leading to loss of ions and inhibition of *Saccharomyces cerevisiae* (Rao et al., 2010). 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 (Carson et al., 2006; Hammer et al., 2004). Mitochondrial membrane permiabilization due to EOs treatment leads to apoptosis and necrosis leading to cell death (Armstrong, 2006). Also, individual constituent of EOs can interfere in TOR signalling pathway of yeasts resulting in loss of viability (Rao et al., 2010). Modulation of the plasma membrane, cytoplasm and nucleus is observed in SEM and TEM analysis of *Phytophthora infestans* treated with plant EOs (Soylu et al., 2006).

5. Cancer preventive properties

One of the most difficult challenges in chemotherapy is treatment of malignant cell growth leading to cancer. Plant molecules like taxol are effective against cancerous cell proliferation. Various types of malignancies like, glioma, colon cancer, gastric cancer, human liver tumour, pulmonary tumours, breast cancer, and leukaemia are reported to be lowered after treatment with plant EOs. Hence such molecules are supposed to have potential anticancer activities to be useful in prevention and therapeutics strategies (Edris, 2007; Kaefer and Milner, 2008; Hamid et al., 2011) (Table 4). 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 (Carnesecchi et al., 2004). β-eudesmol, a constituent of *Atractylodes lancea* oil may find use in prevention of malignant tumours (Tsuneki et al., 2005). Terpenoids as well as polyphenol constituents of plant oils prevent tumour cell proliferation through necrosis or induction of apoptosis (Bakkali et al., 2008; Dudai et al., 2005). Significant hepatoprotective activities have been reported for *Myristica fragrans* (nutmeg) oil (Morita et al., 2003), which may be assigned to its main component, myristicin. Myristicin is supposed to act through induction of apoptosis as displayed in neuroblastoma cells (Lee et al., 2005). Citral present in lemongrass oil is found useful *in vivo* against the early phase of rat hepatocarcinogenesis (Puatanachokchai et al., 2002). *Allium sativum* (garlic) essential oil is well recognized for anticancer properties. The chemopreventive

Table 4
Antitumor and anticancer potential of essential oils.

Sr. no.	Antitumor/anticancer activities	Essential oils	References
1	Inhibition of proliferation of murine leukaemia and human mouth epidermal carcinoma cell lines	*Alpinia officinarum* (Galangal/China root); *Citrus hystrix* (Thai Lime); *C. paradise* (Grape fruit tree); *Curcuma longa* (Turmeric); *Cymbopogon nardus* (Citronella grass); *Cymbopogon martini* (Palmarosa); *Lavandula angustifolia; Mentha spicata; Ocimum basilicum*; *O. americanum*; *O. sanctum*; *Piper nigrum*; *P. betle* (Beetle leaf); *Zingiber montanum; Vetiveria zizanioides* (Khus)	Hata et al. (2003), Carnesecchi et al. (2004), Koo et al. (2004), Manosroi et al. (2006)
2	Induction of apoptosis in cultured hepatocarcinoma cells	*Artemisia annua*	Li et al. (2004)
3	Anti- angiogenesis properties	*Atractylodes lancea*	Tsuneki et al. (2005)
4	Inhibition of primary liver cancer	*Curcuma longa* (Turmeric)	Koo et al. (2004), Manosroi et al. (2006)
5	Induction of apoptosis in human leukaemia cells	*Elettaria cardamomum* (Cardamom); *Eucalyptus globulus* (Eucalyptus)	Juergens et al. (1998), Moteki et al. (2002)
6	Chemoprevention of various cancers	*Allium sativum; Elaeis guineensis* (Palm oil)	Milner (2001), Luk et al. (2011)
7	Inhibition of Proliferation of cancerous cells	*Eugenia caryophyllata (i.e. Syzygium aromaticum)*	Yoo et al. (2005)
8	Hepatoprotective activity	*Foeniculum vulgare; Myristica fragrans*	Ozbek et al. (2003), Morita et al. (2003), Lee et al. (2005)
9	Inhibition of growth of different human cancer cell lines like, breast cancer and liver cancer	*Foeniculum vulgare*	Ozbek et al. (2003)
10	Induction of apoptosis in highly malignant glioma cell	*Matricaria chamomilla*	Cavalieri et al. (2004)
11	Protection against colon cancer	*Glycine max* (Soybean oil)	Yoshiki et al. (1998)
12	Induction of caspase dependent apoptosis in human melanoma	*Melaleuca alternifolia*	Calcabrini et al. (2004)
13	Activity against a series of human cancer cell lines and a mouse cell line	*Melissa officinalis*	De Sousa et al. (2004)
14	Activity against lung and colon cancer cell lines	*Myrica gale* (Myrtle/Bayberry)	Sylvestre et al. (2005, 2006)
15	Induction of apoptosis in human neuroblastoma	*Myristica fragrans*	Morita et al. (2003), Lee et al. (2005)
16	Inhibition of cancer proliferation in rats	*Nigella sativa*	Salim and Fukushima (2003), Mansour et al. (2001)
17	Protection against colorectal cancer	*Olea europaea* (Olive oil)	Gill et al. (2005)
18	Prevention of human cancer cell lines including melanoma, breast and ovarian cancer	*Tetraclinis articulate* (conifer oil)	Buhagiar et al. (1999)

activity is confined to ability of garlic to suppress drug detoxifying enzymes (Chen et al., 2004; Milner, 2001). Growth of a series of human cancer cell lines is inhibited after treatment of lemon balm (*M. officinalis*) oil (Sousa et al., 2004). Induction of apoptosis by *M. alternifolia* (Tea tree) oil and its major monoterpene alcohol, terpinen-4-ol, is related with low incidence of human melanoma (Calcabrini et al., 2004). 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 (Czarnecka et al., 2006).

6. Antiviral efficacy

In addition to the antimicrobial activities, plants are shown to possess notable antiviral properties (Table 5). Inhibition of viral replication is believed to be due to the presence of monoterpene, sesquiterpene and phenylpropanoid constituents of EOs (Astani et al., 2011). Inhibitory activity against herpes virus is reported for eucalyptus and thyme oils (Schnitzler et al., 2007; Reichling et al., 2005). It is found that *M. alternifolia* oil exhibits significant efficacy in the treatment of recurrent herpes virus infections (Carson et al., 2001). This activity was confined to the ability to interfere with viral envelope structures, so that adsorption or entry of virus into the host cells is prevented. For example, oregano oil causes dissolution of the HSV envelope to attenuate its infective ability (Siddiqui et al., 1996). Oregano oil is also known to exert antiviral activity against yellow fever virus at 3.7 μg/ml (Meneses et al., 2009). Isoborneol, a monoterpene from several EOs show virucidal effect on HSV-1, through inhibition of glycosylation of viral proteins (Armaka et al., 1999). German chamomile has been observed to inhibit HSV-1 at concentration as low as 0.00003%. While, santolina, pine, tea tree, manuka and lemon balm oils are efficient against HSV-1 in the concentration range of 0.0001–0.0009%. Comparatively HSV-2 is more sensitive to the above mentioned oils with lower IC_{50} values (Garcia et al., 2003; Saddi et al., 2007; Koch et al., 2008; Schnitzler et al., 2011). EO components are reported to specifically inhibit early gene expression in CMV (cytomegalovirus) and thereby prevent viral activation (Pusztai et al., 2010). A study in mouse model underlined *in vivo* efficacy of eugenol from clove oil to interfere with the development of herpesvirus-induced keratitis (Benencia and Courreges, 2000).

7. Antimutagenic properties

Significant antimutagenic activities have been observed for certain EOs and their components (De Flora et al., 1999; Dahanukar et al., 2000; Jeena et al., 2013; Varona et al., 2013). *Matricaria chamomilla* oil is shown to inhibit daunorubicine and methyl methane sulfonate induced mutagenic errors in mouse bone marrow cells (Hernandez-Ceruelos et al., 2002). *Melaleuca alternifolia* and *L. angustifolia* EOs displayed strong inhibitory potential against mutations induced in *E. coli* model (Evandri et al., 2005). α-Bisabolol (a sesquiterpene in EOs) is reported to exhibit activity against aflatoxin B1, benzopyrene and 2-aminofluorene induced mutagenesis (Gomes-Carneiro et al., 2005). UV induced mutations in *S. typhimurium*; *E. coli* and *S. cerevisiae* are prevented by EO of *S. officinalis* and its major components (Vukovic-Gacic et al., 2006). *Helichrysum italicum, Ledum groenlandicum*, *Cinnamomum camphora* and *Origanum compactum* EOs are reported to be active against the urethane-induced mutations in *Drosophila melanogaster* (Idaomar et al., 2002; Mezzoug et al., 2007). Similarly, protection of chromosomal damage in human lymphocytes by *Curcuma longa*, *Piper betel* and *Acacia catechu* extract mixture is observed *in vitro* (Ghaisas and Bhide, 1994). Hastak et al. (1997) have described the chemo preventive activity of *C. longa* oil on cytogenetic damage to oral sub-mucous cells. Components of *Terminalia arjuna* exhibit anti-mutagenic potential in *S. typhimurium* (Kaur et al., 1997). Antimutagenic effects of EOs may be confined to their ability to inhibit penetration of mutagens inside the cells, free radical scavenging activity, activation of antioxidant enzymes (Sharma et al., 2001; Ipek et al., 2005) and inhibition of P450 mediated formation of mutagens (Gomes-Carneiro et al., 2005). Interference

Table 5
Antiviral activities of essential oils.

Sr. no.	Antiviral effect	Essential oil	References
1	Inactivation of yellow Fever Virus	*Artemisia arborescens*; *A. vulgaris*; *Lippia origanoides* (Wild Marjoram); *Oreganum vulgare*	Siddiqui et al. (1996); Sinico et al. (2005); Meneses et al. (2009)
2	Activity against Herpes Simplex Virus type-1 (HSV-1);	*Artemisia arborescens*; *A. vulgaris; Allium cepa* (Onion); *A. sativum* (Garlic); *Corriandrum sativum* (Cilantro/Dhania); *Cuminum cyminum; Ocimum basilicum*; *O. americanum*; *O. sanctum*	Sinico et al. (2005); Meneses et al. (2009); Romeilah et al. (2010)
3	Activity against HSV-1 & HSV-2	*Eugenia caryophyllata* (*i.e. Syzygium aromaticum*); *Eucalyptus globulus* (Eucalyptus oil); *Leptospermum scoparium* (Manuka oil); *Melaleuca alternifolia; M. armillaris*; *Oreganum vulgare*; *Santalum* sp. (Sandalwood)	Bishop (1995), Siddiqui et al. (1996), Benencia and Courreges (1999, 2000), Schnitzler et al. (2001), Reichling et al. (2005), Cermelli et al. (2008), Garozzo et al. (2009), Meneses et al. (2009)
4	Activity against Respiratory viruses	*Eucalyptus globulus* (Eucalyptus oil)	Schnitzler et al. (2001), Cermelli et al. (2008)
5	Anti-HIV effect; prevention of RNA and DNA viruses	*Glycyrrhiza glabra* (Licorice)	Lalita (1994), Watanbe et al. (1996)
6	Virucidal effect on influenza virus & HSV-1	*Houttuynia cordata* (Fishwort/Chameleon plant); *Melaleuca alternifolia*	Hayashi et al. (1995), Garozzo et al. (2009, 2011)
7	Inhibition of HSV-1 replication	*Cymbopogon citrate* and other species	Minami et al. (2003)
8	Virucidal activity against HSV-1 & HSV-2	*Mentha piperita*	Schuhmacher et al. (2003)
9	Antiviral activities	*Salvia fructicosa*	Sivropoulou et al. (1997)
10	Prevention of Replication of HSV-2	*Melissa officinalis* L.	Allahverdiyev et al. (2004)
11	Inactivation of viral particles of HSV-1 & HSV-2	*Santolina insularis*	De Logu et al. (2000)
12	Inhibition of replication of Epstein–Barr virus (EBV)	*Thymus* sp.	Hamid et al. (2011)

with mutation inducing DNA repair systems (Vukovic-Gacic et al., 2006) and induction of necrosis/apoptosis leading to cellular death are among the proposed mechanisms behind antimutagenic activity of essential oils (Bakkali et al., 2008).

8. Essential oils as antioxidants

Oxidative stress due to generation of free radicals and reactive oxygen species (ROS) cause damage to cellular macromolecules (McCord, 2000). Oxidative damage has been related to various health problems such as ageing, arteriosclerosis, cancer, Alzheimer's disease, Parkinson's disease, diabetes and asthma (Edris, 2007). Cellular balance of free radicals is mantained by different antioxidants. Flavonoids, terpenoids and phenolic constituents of EOs exhibit significant antioxidant effects (Tomaino et al., 2005, Ferguson and Philpott, 2008; Miguel, 2010; Cavar et al., 2012; Sanchez-Vioque et al., 2013). For example, *Origanum majorana*, *Tagetes filifolia, Bacopa monnierii* and *C. longa* oils have pronounced antioxidative capacities (Maestri et al., 2006; Tripathi et al., 2007; Maheshwari et al., 2006). The EOs of *Salvia cryptantha* and *S. multicaulis*, *Achillea millefolium*, *M. officinalis*, *M. alternifolia*, *Curcuma zedoaria*; *Ocimum* sp. and *Mentha* sp. possess potential antioxidant or free radical scavenging activity (Gulluce et al., 2007; Hussain et al., 2008; Kim et al., 2004; Mau et al., 2003; Politeo et al., 2007; Tepe et al., 2004). Two main ingradients of *Thymus and Origanum* EOs, thymol and carvacrol, are shown to act as strong antioxidants (Miguel, 2010; Tepe et al., 2004). Similarly, *C. sativum*; *A. sativum*; *A. cepa*; *Cuminum cyminum* and *Petroselinum sativum* have potent free radical scavenging activity (Romeilah et al., 2010). 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 (Tomaino et al., 2005).

9. 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 (Marles and Farnsworth, 1995; Dahanukar et al., 2000). Comparatively, less information is available on diabetic preventive efficacy of plant EOs (Hamid et al., 2011). Selected EOs are reported to exhibit preventive effects on diabetes associated health hazards (Broadhurst et al., 2000; Misra and Dey, 2013). Few *in vivo* studies are also available like, antidiabetic effects of rosemary oil in hyperglycemic rabbits (Al-Hader et al., 1994). 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 above mentioned combination of EOs (Talpur et al., 2005). Similarly, *Satureja khuzestanica* oil causes significant decrease in fasting blood glucose levels in diabetic rats (Abdollahi et al., 2003). However, the mechanisms involved behind antidiabetic potential of plant EOs are not well elucidated.

10. Anti-inflammatory activities

Essential oil of *Ocimum sanctum* is known to possess activity against inflammatory reactions since a long time (Singh and Majumdar, 1997). Other examples of plant EOs with anti-inflammatory activity are *Baphia nitida* (Onwukaeme, 1995), *L. angustifolia*, *Mentha* sp. and *Eucalyptus* sp. (Gulluce et al., 2007; Hajhashemi et al., 2003; Moreno et al., 2002; Silva et al., 2003). Eucalyptus, rosemary, lavender, pine, clove and myrrh oils exert potential inflammation preventive abilities (Darshan and Doreswamy, 2004; Barbieri Xavier et al., 2013). During the oxidative burst of inflammatory reaction there is formation of reactive oxygen species (ROS). Among various mechanisms known to be involved in inflammation preventive activity of EOs, the free radical scavenging efficacy is considered as important (Miguel, 2010). EOs of Aloe-vera (*Aloe barbadensis*), anise star (*Illicium verum*), bergamot (*Citrus aurantium*), cinnamon leaf (*Cinnamomum zeylanicum*), juniperus berry (*Juniperus communis*), lavender (*Lavandula officinalis*), thyme (*T. vulgaris*) and ylang-ylang (*Cananga odorata)* possess anti-inflammatory potential. Their activities are mediated through mechanisms such as, inhibition of lipoxygenase, prevention of leukotriene synthesis, inhibition of COX-2 enzyme, inhibition of pro-inflammatory cytokines, interleukin-1β (IL-1 β) and tumour necrosis factor-α (TNF-α), as well as reppression of pro-inflammatory genes (Miguel, 2010).

11. 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 (Sauter et al., 2012). Hence new options for treatment of protozoal diseases are being searched. For a long time, followers of traditional medicines were prescribing plant extracts and EOs as remedies for protozoal diseases (Cowan, 1999; Sauter et al., 2012). These activities have been confirmed with the modern scientific approaches. For example, oregano (*O. vulgare*), *Nepeta cataria* and *Lippia alba* oils are known to readily inhibit the growth of trypanosomal parasite by causing cell lysis. *Thymus vulgaris* and its major component thymol are shown to possess anti-trypanosomal effect through destabilization of plasma membrane (Santoro et al., 2007; Saeidnia and Gohari, 2012). 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*. Their anti-amoebic potential is attributed to the terpenoid components like, thymol, carvacrol and linalool (Vunda et al., 2012). Growth and adherence of *Giardia lamblia* is prevented by *Thymbra* capitata, *Origanum virens*, *Thymus zygis* subsp. Sylvestris, *O. basilicum* and *Lippia graveolens* oils. Treatment with these oils result in ultra structural changes in cells leading to loss of viability (Almeida et al., 2007; Machado et al., 2010). *Melaleuca alternifolia, Carum copticum* and *L. angustifolia* EOs and their phenolic constituents exhibit antiprotozoal effects (Carson et al., 2006; Mansoor et al., 2011). Anti-plasmodial activity of plant EOs is reported by various workers (Milhau et al., 1997; Dell'Agli et al., 2012). Among various active oils promising antimalarial potential is attributed to *Cymbopogon citrates*, *Origanum* spp., *Lippia* multiflora, *Ocimum gratissimum* and *Satureja thymbra* oils (Tchoumbougnang et al., 2005; El Babili et al., 2011). Few of the studies have evaluated and discussed the leishmania inhibitory efficacy of oils extracted from *Achillea millefolium*, *Artemisia abrotanum, Chenopodium ambrosioides, Croton cajucara, C. citrates*, *O. gratissimum*, *Pinus caribaea, Piper* sp. (Santos et al., 2010; Santin et al., 2009; Ahmed et al., 2011; Tariku et al., 2011). Among the antileishmanial EOs, particularly *C. cajucara* oil is found to be the most effective with MIC of 85 pg/ml. Its main component linalool is active at a concentration as low as 22 pg/ml (Maria do Socorro et al., 2003). Similarly, *C. ambrosioides* exhibit better activity than other oils with the MIC 27.82 μg/ml (Monzote et al., 2007).

12. Toxicity issues

Essential oils constitute various active molecules hence affect multiple targets in a cell (Carson and Hammer, 2011). 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 (Bakkali et al., 2008). Essential oils can exert cytotoxic effects on eukaryotic cells. Permeabilization of outer and inner mitochondrial membranes causes the cell death by necrosis and apoptosis (Armstrong, 2006). Generally alcohol, aldehydes and phenolic constituents are responsible for the cytotoxicity of EOs (Bruni et al., 2004). This cytotoxic property is important for the chemotherapeutic applications of EOs against a variety of virus, bacteria and fungi (Burt, 2004; Rota et al., 2004; Hammer and Carson, 2011). However, toxicity to eukaryotic cells is also responsible for the undesirable side effects towards host. The risk of various toxic effects such as irritation and corrosiveness, sensitization of cells, percutaneous absorption, acute toxicity to organ system, phototoxicity, carcinogenicity, and teratogenicity limit the medicinal use of EO. 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 (Vigan, 2010).

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. Studies on the toxicity of EOs are available in the form of simple case reports and animal studies (calculation of LD 50) for an EO or a purified constituent (Reichert-Penetrat et al., 1999). Many EOs were found deadly to household mammalian pets. For example, *Mentha pulegium* oil can cause internal bleeding and damage to lungs in dogs leading to death (Sudekum et al., 1992). The toxic effects of ketone terpenoids are known since a long time. Estragol present in the essential oils of tarragon, star anise, green anise, basils and fennels is demonstrated to have carcinogenic effect. 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 (Gordon et al., 1982; Vigan, 2010). 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 (Vigan, 2010).

Essential oils may be safe at low concentrations, but display toxicity to humans at high concentrations represented as lethal dosages (Sinha et al., 2014). 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. Essential oil with citral as the major component is shown to cause histological cell necrosis and vacuolization (Hayes and Markovic, 2003). Ingestion of limonene can cause diarrhoea and transient proteinuria in healthy volunteers (Vigan, 2010). 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, β-asarone and allyl isocyanate respectively have toxic effects in humans (Dweck, 2009). 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 (Vigan, 2010). Clove oils (*S. aromaticum*), coriander oil (*C. sativum*) with high linalool content, melissa oil (*M. officinalis*), origanum oil (*O. vulgare*), summer savoury oil (*S. hortensis*), tea tree oil (*M. alternifolia*), thyme oil (*T. vulgaris*) and turpentine oil (*Pinus sylvestris*) exposure are known to act as irritants. Some of the EOs like bergamot oil (*C. aurantium*), cumin oil (*C. cyminum*), grapefruit oil (*Citrus paradisi*), lime oil (*Citrus limon*) and orange oil (*Citrus sinensis*) induce phototoxicity in humans (Dijoux et al., 2006; Dweck, 2009).

Similarly, spanish sage oil (*Salvia lavandulaefolia*), dill seed oil (*A. graveolens*), savin oil (*Juniperus sabina*) and wormwood oil (*A. absinthium*) are among few of the EOs which were noticed as toxic 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 (Dweck, 2009). Calamus oil (*Acorus calamus*) containing β-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 (Bakkali et al., 2008). 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 (Sinha et al., 2014). Therefore, it is advisable that EOs should be used very carefully with considerable precautions about the concentrations being used, product application (route of administrations), 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 (Nakatsu et al., 2000).

13. Essential oils with economic importance in medicinal industry

Use of plant EOs for perfumery, additives in food/confectionary as well as for pharmaceuticals and cosmetics is a growing market trend. A rapid increase has been observed in the number of essential oil derived products. 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. Essential oils have been an important part of the medicinal industry throughout the twentieth century (Cragg et al., 1997). Their use as aromatherapy products, traditional systems of medicines and in complementary systems of medicines is increasing consistently in USA, Europe, Africa and in Asian countries. The main components of this hundreds of million dollar industry are pharmaceuticals, medicinal supplements, and nutriceutical companies (Nakatsu et al., 2000; Hussain et al., 2008; Teixeira et al., 2013).

The huge production of EOs (>70,000 tonnes per anum) 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 are

other examples. It is not surprising that these countries also represent the main market for the particular EOs (Bedi et al., 2010). Approximately 300 EOs are considered important from the commercial point of view (Bakkali et al., 2008). EOs which have highest production and market value worldwide can be mentioned as, orange oil (*C. sinensis*), corn mint (*Mentha arvensis*), peppermint (*Mentha* sp.), eucalyptus (*E. globulus*), citronella (*Cymbopogon* sp.), lemon (*C. limon*), clove (*S. aromaticum*) and camphor (*C. camphora*). This is followed by basil, clary sage, lavender, sage, thyme, tarragon, chamomile, wormwood, coriander, fennel, dill, celery, anise, ajowan and cumin oils (Hussain et al., 2008; Bedi et al., 2010). 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 $30 per pound. Comparatively calendula, thyme, dill, summer savoury may cost very high (*i.e.* >$ 100 per pound weight of the oil). Retail prices for caraway, fennel, clary sage, lavender and sweet basil oils can be $ 50 to $ 80 per pound (Brester et al., 2002).

Many of these have potential to be used in medicinal industry. Particularly, EOs obtained from plants belonging to family Apiaceae, Lamiaceae, Myrtaceae, Poaceae, Rutaceae are important from the point of view of medicinal applications. 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 (Hammer and Carson, 2011; Hussain et al., 2008; Bedi et al., 2010). 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 (Hammer and Carson, 2011).

14. Conclusions and promises

Efforts are being done to further explore the enormous range of biological activities of essential oils and their potential industrial applications. Novel approaches of chemotherapy and chemoprevention are necessary in the advent of multiple drug resistance related with infectious and noninfectious 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 (Edris, 2007; Vigan, 2010). Use of plant molecules for prophylaxis and treatment of infectious and noninfectious diseases can be a good strategy (Raut et al., 2013c). The 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. Selected molecules from some of these EOs have been granted GRAS (Generally Regarded as Safe) status by Food and Drug Administration of USA (Raut et al., 2013a,b). Certain advantages associated with the use of EOs are less toxicity, reduced genotoxicity (even after prolonged use), ability to act on multiple cellular targets and low cost of production. Many of the plant molecules possess an ability to act as chemosensitizers when used in combination and enhance activity of the partner drug. Synergy research is actively analysing efficacy of EOs and individual components in combination with already existing drugs so that required dosages of drugs can be significantly reduced (Wagner and Ulrich-Merzenich, 2009). Also, combination of two different EOs may result in considerable enhancement of the activity compared to the individual oils. Internal synergy has been well documented for the insecticidal properties of EOs (Jiang et al., 2009). There is need to analyze and document such internal synergy trends for 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. These molecules may act as scaffolds to build novel molecules for therapeutics and offer tremendous scope for further research. Efforts need to be directed towards use of automation and highthroughput screening to search for novel bioactivities of EOs. In addition, the huge information being generated by *in vitro* assays need to be confirmed through systematic animal studies and clinical investigations.

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