# Antimicrobial and synergistic effects of some essential oils to fight against microbial pathogens – a review

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There is a global increase in the occurrence of fungal and bacterial infections and development of microbial resistance to antibiotics is a global concern. Apart from infectious diseases, food spoilage also occurs because of contamination caused by microorganisms. The quality, taste, colour, flavour and shelf life of food is decreased. The best way to solve this problem is the use of natural compounds especially essential oils. One tactic employed to overcome the resistance mechanisms is the use of plant extracts or essential oil singly or in combination i.e. synergistic approach. Synergistic effects may be due to certain complex formations that become more effective in the inhibition of microorganisms. It has been reported that several medicine plants, spices and especially herbs containing essential oils significantly inhibited a broad range of microorganisms. Essential oils are the volatile oily liquids of the secondary metabolism of plants which are obtained from almost all plant parts like flowers, buds, leaves, stems, seeds, bark, fruits and roots. Essential oils can be individually effective or they may be combined with antibiotics or plant extracts. Traditional healers often use combinations of plants to treat or cure diseases and found that synergy was most often quite promising. This review describes some promising medicinal plant essential oils and their synergistic effects. This may be a novel approach with promising results to deal with multi drug resistant microorganisms and new ways of treating resistant bacteria and fungi.

**Keywords:** Drug resistances; Antibiotics; Essential oil; Antimicrobial activity; Synergistic effects

## 1. Introduction

The emergence of microbial resistance to multiple antimicrobial agents has become a significant global concern. Microorganisms resistant to more than two groups of antibiotics are regarded as multi-drug resistant (MDR). The global emergence of MDR bacteria is gradually elevated morbidity and mortality rates as well as in the increased treatment costs which limit the effectiveness of existing drugs and significantly cause treatment failure [1,2]. It often stops to respond to conventional antimicrobial agents and treatment, resulting in adverse effects on the patients, greater threat of death and higher costs [3]. Hospital acquired infections caused by MDR bacteria is major challenge for clinicians and it creates problems in cancer and AIDS patients. Most widespread multidrug resistant bacteria include Gram-positive methicillin- resistant, *Staphylococcus aureus*, enterococci and Gram-negative bacteria i.e. members of Enterobacteriaceae and others like *Pseudomonas aeruginosa*, *Mycobacterium tuberculosis* [4]. The most wide spread multidrug resistant fungal pathogens which cause the nosocomial infections belonging to the genera *Candida*, *Aspergillus*, *Rhizopus*, *Penicillium*, *Fusarium, Cryptococcus* and *Mucormycoses* show high resistance to antifungal agents [5, 6].

The indiscriminate exposure of antibiotics caused resistance and this imposed microorganisms to have a superior ability to stay alive even the strongest antibiotics [7]. Therefore, it becomes necessary to enforce and implement some measures to reduce this problem of MDR; it can be achieved by some actions like to control the use of antibiotics, understand the genetic mechanisms of resistance, continue search for drugs with novel mechanisms of action, either synthetic or natural and take accuracy of diagnostic procedures or reduce the length of treatment [8]. In current scenario, number and types of infectious diseases are increasing at an alarming rate. This knowledge of risk associated with the use of antimicrobial agents or antibiotics has prompted research to explore medicinal properties of plants and their extracts which can serve as herbal sources of antimicrobial agents for protection against a wide range of bacteria (Gram-negative and Gram-positive) including antibiotic resistant species and fungal species [9, 10]. Plants contain active metabolites which may serve as alternative source of folk medicines and useful in treating various infectious diseases [11]. Plant secondary metabolites and essential oils can be used as an alternative remedies for the treatment of many infectious diseases.

## 2. Essential oils

Essential oils are the volatile liquids of the secondary metabolism of aromatic plants. They are termed “essential” because they represent the most important part of the plant. They are synthesized by all plant organs such as flowers, leaves, stems [12], seeds [13], barks [14], fruits [15], roots [16], peels [17] and are stored in secretory cells, cavities, canals, epidermal cells or glandular trichomes [18, 19]. Essential oils are not limited to a particular class or family of plants but they are widely distributed in all plant kingdom. The essential oils are found in plants belonging to the families like, Asteraceae, Aristolochiaceae, Cupressaceae, Fabaceae, Lamiaceae, Lauraceae, Meliaceae, Myrtaceae, Rutaceae, etc.

The essential oils are complex mixers comprising of many single compounds. Chemically they are derived from terpenes and terpenoids (isoprenoids) and aromatic and aliphatic aldehydes and phenols, all characterized by low molecular weight [20]. Each of these constituents contributes to the beneficial or adverse effects [21]. There are many methods of extraction of essential oils. They can be obtained by steam distillation, mechanical expression, hydro distillation, fermentation or extraction but the method of steam distillation is most commonly used for commercial production. During distillation, water condensate and is separated by gravity leaving a very small amount of volatile liquid that is the essential oil [22]. Due to their extraction procedure, they contain a variety of volatile molecules such as terpenoids, terpenes, aromatic compounds and aliphatic components [23].

The use of essential oils as function of ingredients in foods, drinks and cosmetics is gaining force, both for the rising interest of consumers in use of natural ingredients and also increasing concern about potentially unsafe of synthetic additives [24]. Essential oils are commercially important especially for the pharmaceutical, agronomic, food, sanitary, cosmetic and perfume industries [23, 25]. Essential oils exhibit various biological activities like antibacterial [26, 27, 28], antifungal [29, 30], antiviral [31, 32], insecticidal [33] antioxidant [34, 35, 36], anticancer activity [37, 38, 39], anti-inflammatory [40, 41, 42], Anti-staphylococcal activity [43], Antimycotic activities [44] and antidiabetic [45, 46, 47], etc. Some oils are also used in food preservation, aromatherapy [48] and fragrance industries [49].

## 3. Antimicrobial activity of essential oils

Essential oils and their constituents significantly inhibit a wide range of microorganisms including human and phytopathogens, food spoilage and poisoning bacteria. Essential oils and extracts from several plant species are able to control microorganisms related to skin, dental caries and food spoilage, including Gram-negative and Gram-positive bacteria, fungi and viruses [50, 51, 52]. The essential oils are very well known for their bactericidal, bacteriastatic, virucidal, fungicidal activity due to their medicinal properties against the wide range of pathogenic microorganisms [53]. However, the spectrum of antimicrobial activity is dependent on the tested pathogens, measurement conditions and the source of the antimicrobial compounds [54]. Antimicrobial effects of different species of herbs and spices have long been known and used to increase the shelf-life of food. Thus the essential oils and their components, currently used as food flavorings are also known to possess antimicrobial activity [55].

Now-a- days, clinically important microorganisms are characterized not only by single drug resistance, but also by multiple drug resistance. It is now common practice to use a combination of two or more antibiotics with different mode of action in an effort to prevent the expansion of antibiotic resistance and improve the outcome of therapy [56]. Synergistic effects of antimicrobial agents may be due to certain complex formations that become more effective than individual in the inhibition of microorganisms. Synergistic antimicrobial activity between essential oil and antimicrobial agents are one of the new ways to inhibit multidrug resistant bacteria. Such combination therapy could lead to a reduction of the minimum effective dose of the antibiotics needed for treatment, to reduce side effects [43, 57], to obtain synergistic antimicrobial activity and expand the antimicrobial spectrum [22, 58]. So in the present review, some of the most promising essential oils plants are listed along with the part used, organisms tested, method used, mode of action, etc is given in Tables 1 and their synergistic effects is given in Table 2 and some of them are discussed below.

### 3.1 Antibacterial activity of essential oils

Sun *et al.,* [59] reported antibacterial activity of root essential oil of *Dictamnus angustifolius* against the *Staphylococcus aureus, Escherichia coli* and *Pseudomonas aeruginosa.* Burt and Reinders, [60] analyzed the antibacterial properties of five essential oils bay (*Pimenta racemosa*), clove bud (*Eugenia caryophyllata*, *Syzygium aromaticum*), oregano (*Origanum vulgare*), red and light thyme oils (*Thymus vulgaris*) against *Escherichia coli* O157:H7strain. Oregano and light thyme essential oils had the potential of preventing the growth of *E. coli* O157:H7 in foods.

Pirbalouti *et al.,* [61] observed the antibacterial activity of essential oil of *Myrtus communs* from leaves of five wide populations against animal borne diseases causing bacteria *Erysipelothix rhusiopathiae.* They have concluded that essential oil from various populations showed high degree of inhibitory activity and population-VI showed highest antibacterial activity. Ghalem and Mohamed, [62] found that *Eucalyptus camaldulensis* leaves essential oil showed good antibacterial activity against *Escherichia coli* and *Staphylococcus aureus.*

Sousa *et al,.* [63] reported antimicrobial activity of essential oil and its four fractions from *Eugenia calycina* Cambess. leaves against oral bacteria. The results showed that essential oil exhibited strong antibacterial activity against anaerobic Gram-negative bacteria *Prevotella nigrescens* and *Porphyromonas gingivalis* and Fraction 3 and Fraction 4, composed of oxygenated sequiterpenes showed higher activity against all the bacteria. Falsafi *et al.,* [64] observed the anti-*Helicobacter pylori* effect of *Satureja bachtiarica* Bunge essential oil. The results showed that essential oil significantly inhibited the growth of clinical isolates of *Helicobacter pylori.*

### 3.2 Antifungal activity of essential oils

Prakash *et al.,* [65] reported good antifungal activity of *Piper betle* L. essential oil against different fungal isolates. Gazim *et al.,* [66] showed *Calendula officinalis* flower essential oil effective against 23 clinical fungal isolates tested even better than commercial antifungal agent Nystain. Amber *et al.,* [67] analyzed synergistic antimicrobial activity of *Ocimum sanctum* essential oil in combination with fluconazole and ketoconazole against fungal strain *Candida*. The results showed that this combination showed potent *in vitro* antifungal effects against *Candida* isolates, including fluconazole resistant. Taweechaisupapong *et al.,* [10] reported post antifungal effect of lemongrass oil on clinical isolate *Candida dubliniensis*. Samber *et al.,* [68] found significant antifungal activity of *Mentha piperita* essential oil and its major constituents Menthol, Carvone and Menthone against *Candida albicans, Candida tropicalis* and *Candida glabrata.* Vieira *et al.,* [69] reported antifungal effect of essential oils from five *Ocimum* species*.* Among the five plants *Ocimum micranthum* and *Ocimum selloi* showed the best results due to the presence of effective antifungal compounds eugenol and anethole. The essential oil of *Thymus vulgaris* L. showed good antifungal activity against *Rhizopus oryzae* [6]. The antifungal activity of *Eugenia caryophyllata* essential oil was reported against 53 clinical isolates of *Candida* by Chaieb *et al.*, [70].

### 3.3 Antiviral activity of essential oils

Gilling *et al.* [71] reported antiviral efficacy of oregano essential oil and its main constitutant carvacrol against the nonenveloped *Murine norovirus*. The results demonstrated that carvacrol is potent in inactivating *Murine norovirus*. Orhan *et al.,*[72] screened some essential oils and their constituents for their antiviral activity against *Herpes simplex* type-1 and *Para influenza* type-3. The results showed that most of the oils and compounds displayed strong antiviral effects against HSV-1, ranging between 0.8 and 0.025 µg/ml. Elaissi *et al.,* [73] evaluate the antiviral activity of 8 *Eucalyptus* species essential oils against coxsakie virus B3. The results showed that essential oil of *E. astringens* exhibited significant antiviral activity only when incubated with virus prior to cell infection and also showed effective antimicrobial activity.

### 3.4 Synergistic antimicrobial activity of essential oils

Lv *et al.,* [74] examined the effectiveness of plant essential oil combinations against four food-related microorganisms. The results stated that four kinds of essential oil combinations showed synergistic antimicrobial activity i.e. oregano–basil for *E. coli,* basil–bergamot for *Staphylococcus aureus,* oregano–bergamot for *B. subtilis* and oregano–perilla for *S. cerevisiae.* Rapper *et al.,* [75] analyzed the antimicrobial activity of *Lavandula angutifolia* essential oil in combination with other 45 essential oils against pathogenic microorganisms like *Staphylococcus aureus, Pseudomonas aeroginosa*, and *Candida albicans* and stated that these oil combinations showed 26.7% synergistic and 48.9% additive effects against pathogens. Matan *et al.,* [76] reported that mixture of cinnamon and clove essential oils showed inhibitory activity against food spoilage microorganisms. *C. rubum* and *E. coli* were the most susceptible bacterial pathogens.

Nguefack *et al.*, [77] observed synergistic effect of essential oil fractions from *Cymbopogon citratus, Ocimum gratissimum* and *Thymus vulgaris* against *Penicillium expansum.* The results showed that among the 23 mixtures of essential oil fractions tested, 4 mixtures displayed synergistic effect. These combinations increased the antimicrobial activity and reduced the concentration of essential oil required for antimicrobial activity. Magi *et al.,* [78] evaluated the *in vitro* antibacterial activity of *Origanum vulgare, Thymus vulgaris, Lavandula angustifolia, Mentha piperita*, and *Melaleuca alternifolia* essential oils and carvacrol, and synergy of carvacrol and erythromycin, against 32 clinical, erythromycin-resistant Group A *Streptococci*. The results found that thyme and origanum essential oils demonstrated the highest antimicrobial activity with lower Minimum Inhibitory Concentration value and combination of carvacrol with erythromycin showed potential synergistic antibacterial activity.

## 4. Mechanism of action of essential oil

Mechanism action of essential oils varied from different part of plant and various active constituent present in them. Different compounds present in the essential oils have different mode of action and different biological effects, i.e. antibacterial, antifungal, antiviral and cytotoxicity, effects. There are some commonly accepted mechanisms of action of essential oil in the antimicrobial interaction. The mechanism of action of essential oil involves so many targets in the cell due to large number of active constituent. The antimicrobial actions of essential oils was the inhibition of a common biochemical pathway, inactivate microbial enzyme [79], leaking of cell membrane and increased the membrane permeability [80, 81]. Essential oils may disrupt the structure of different fatty acids, polysaccharides, and phospholipids layers present in the cell wall and cytoplasmic membrane [18, 82]. Essential oils can cause disruption of membrane in microorganisms by the action of lipophilic compounds in the oils and thereby imparting antibacterial activity [83].

The antimicrobial or antifungal mode of action of essential oils may be due to terpenoids, including monoterpenes, sesquiterpenes and their oxygenated derivatives. These compounds are highly lipophilc and are of low molecular weight which disrupt the cell membrane, cause the cell death and also effective in inhibition of sporulation and germination of food spoilage fungi [29].

The essential oils are complex mixtures of large number of molecules, the synergistic antimicrobial activity of essential oils are the result of a synergism of all molecules. The main constituents of certain essential oils are terpineol, monoterpene, eugenol, safrole, thymol, carvacrol, eucalyptol, geraniol, citronellol, limonene, cinnamaldehyde which are responsible for various pharmacological activities. These major components have different mode of action and activity is dependent on the concentration of component, which combination of component have been used and which main molecules are present at the highest levels in mixture [23]. The most important feature is distribution of essential oils in the cell which determines the different type of reactions and biological reposes induced in the cell. The concept of drug synergism appears to be more meaningful when whole essential oils are studied rather than their individual components of the essential oil. Essential oils have not only the ability to inhibit bacterial growth activity, but also to reduce the required active concentration of antibiotics by their synergistic activity. Guerra *et al.,* [84] found that essential oil from *Cinnamomum zeylanicum* and *Citrus limon* showed a synergistic effect in combinations with amikacin against *Acinetobacter baumannii* strains. It is also possible that sometimes the essential oils themselves may not possess compounds that show antimicrobial activity but can operate in synergy with antibiotics or other plant extracts and are able to sensitize the microorganisms which are ineffective to antibiotics [85].

## 5. Methods used for antimicrobial activity

Currently, there is no standardization of the methodology to evaluate the inhibitory activity of essential oils as well-established as for antibiotics [86]. For antibiotics, various methods have been employed to determine the minimum inhibitory concentration (MIC): disk diffusion test, agar dilution test and broth microdilution test, etc. There are a number of methods used to detect synergistic antimicrobial activity however, the checkerboard and time-kill curve methods are the most widely used techniques and the former is relatively easy to perform and monitor [87].

A number of plant essential oils showing various antibacterial and anti fungal activities is given in Table 1. It includes plant part used, microorganisms used and activity of some essential oil. A list of essential oils/antibiotics/solvent extracts combinations showing synergistic effects against a panel of microorganisms are given in Table 2.

**Table 1** List of essential oils plant, part used, microorganisms used, and GC/MS analysis of oil for antimicrobial study.

| Plant name | Part used | Activity | Microorganisms | GC/MS | Reference |
|---|---|---|---|---|---|
| *Melissa offinalis* | Aerial parts | Antimicrobial, Antifungal | PA, EC, SE1, ST, Ss, SL, MF, SA, SE, BC, CA, EF, MC, TT, TR, TM | No | [88] |
| *Ocimum basilicum*<br>*Ocimum vulgare*<br>*Thymus vulgaris* | Aerial parts | Antimicrobial, Antifungal | PA, EC, ST, Ss, MF, SL, SA, SE, BS | Yes | [19] |
| *Thymus saturejoides* | Aerial parts | Antibacterial | EA, EC, KP, PA, BS, BC, ML, SA | No | [89] |
| *Cupressus sempervirens* | Aerial parts | Antimicrobial | BC, BS, EF, SM, SA, AH, EC, KP, PV, PA, SI, CA, SC | No | [90] |
| *Eugenia uniflora* | Leaves | Antibacterial, Antifungal | LM, SA, SD, PA, SE, AH | Yes | [91] |
| *Limoniastrum guyonianum* | Roots, Stems, Leaves, Flowers | Antimicrobial | EC,PA,MI, SE,SA | Yes | [92] |
| *Eucalyptus camaldulensis*<br><br>*Myrtus communis* | Leaves | Antibacterial | SA, LM, ED, ST, EC, PA, BS | Yes | [24] |
| *Juniperus phoenicea* | Leaves | Antimicrobial | BS, BC, SA, LM, EC, PA, KP | Yes | [55] |
| *Clausena anisata* | Leaves | Antimicrobial | EC, SA, ST, Ss, PS, PA | Yes | [52] |
| *Chaerophyllum macropodum* | Leaves and Flowers | Antimicrobial | PA, SD, SE, KP, SA, BS, PV, EC, SP | Yes | [93] |
| *Ferula heuffelii* | Under ground parts | Antimicrobial | SA, SE, ML, MF, EF, EC, KP, PA | Yes | [94] |

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|---|---|---|---|---|---|
| *Zataria multiflora* | Aerial parts | Antimicrobial | BS, SE, PA, EC | Yes | [95] |
| *Eucalyptus camaldulensis* | Leaves | Antibacterial | EC, SA | No | [62] |
| *Myrtus communis* | - | Antimicrobial | SP, SM, CA, AC, PG | No | [96] |
| *Anaphalis lacteal* | Grass | Antibacterial, | SA, BS, BC, EC, ST, PA, AN, SC, PA, FO | Yes | [97] |
| *Cicuta virosa* | Fruits | Antifungal | AF, AO, AN, AA | Yes | [29] |
| *Mesembryanthemum edule* | Leaves | Antifungal | CA, CK, CR, CG, CN | Yes | [98] |
| *Thapsia minor* | Aerial parts | Antifungal | CN, CG | Yes | [99] |
| *Origanum vulgare* | Aerial parts | Antimicrobial | MS, EC, LM, ML,PA,SA,SF, CA | Yes | [100] |
| *Asarum heterotropoides* | Aerial parts | Antifungal | AH, CG, RSO, PPC, FSo | Yes | [101] |
| *Cinnamomum verum* | - | Antimicrobial | EC, YE, PA, SC, SA, LM, BC, EF | Yes | [102] |
| *Cinnamomum verum* | - | Antibacterial | EC, SA | No | [103] |
| *Cinnamomum verum* | - | Antimicrobial | AF, PR, MP, ES, DH, PM, ZR, CL, SA, PH | No | [76] |
| *Syzygium aromatic* | Roots | Antimicrobial | EF | No | [16] |
| *Syzygium aromatic* | Fruits | Antimicrobial | LI, EC | No | [104] |
| *Caryophyllus aromaticus* | Fruits | Antimicrobial | LM, SA, BS, EF, BC, PA, SM, CF, EC, KP | No | [15] |
| *Citrus sinensis* | Peels | Antimicrobial | SA | No | [105] |
| *Citrus sinensis*<br>*Citrus lemon*<br>*Citrus reticulata*<br>*Citrus paradisi* | Peels | Antifungal | AN, AF, PC, PV | No | [106] |
| *Citrus sinensis* | Peels | Antimicrobial | SA, EF, EC, PA, CA | Yes | [107] |
| *Azadirachta indica* | Leaves and bark | Antimicrobial | ST, EC, VC, BS | No | [14] |
| *Azadirachta indica* | - | Antibacterial | EC | No | [108] |
| *Azadirachta indica* | - | Antimicrobial | PA | No | [109] |
| *Citrus limon* | Peels | Antimicrobial | SA, EC | No | [17] |
| *Mentha piperita* | Seeds | Antimicrobial | SA, PA, CA, AN | No | [13] |
| *Mentha piperita* | Leaves | Antibacterial | BC, EF, SP, SA, EC, PV, KP, PA, SM | No | [27] |
| *Eucalpytus citriodora* | Leaves | Antibacterial | EC, SA, PM, PV, ST, EA, PA, PT, AF, BC, CF, | No | [26] |
| *Daucus carrot* | - | Antimicrobial | LM, SA, SE, ST, EC, SD, AN | Yes | [110] |

 

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|---|---|---|---|---|---|
| *Origanum syriacum* | Whole plant | Antibacterial | SA, EC, PA, EF | Yes | [111] |
| *Cinnamomum Zeylanicum* | - | Antimicrobial | SE, EC, BS, KP, PA | Yes | [112] |
| *Citrus limon* | Peels | Antimicrobial | LM, SA, SE2, EnS | No | [113] |
| *Teucrium polium* | - | Antibacterial | PAG, BN, RR, RV, RS, SSC, XC, PC | No | [114] |
| *Ocimum gratissimum* | - | Antifungal | AF, AN, AFu, AT, FN, ASy, AA, PI, CL, Cs | Yes | [115] |
| *Cuminum cyminum* | Seeds | Antimicrobial | EC, SA, SF, PA, KP | Yes | [116] |
| *Thymus vulgaris*<br>*Eucalyptus globulus* | Aerial parts | Antibacterial | BC, EC, KP, SA, MRSA | No | [57] |
| *Senna podocarpa* | Leaves | Antimicrobial | BS, SA, EC, Ks, PRs, Ps, SLs, PN, RF | No | [117] |

**Table 2** List of essential oils/antibiotics/solvent extracts combination showing synergistic effects against a panel of microorganisms.

| Pair combinations | Microorganisms | Methods | Interaction | References |
|---|---|---|---|---|
| *T. maroccanus &broussonetii/C*iprofloxacin<br>*T. maroccanus & broussonetii*/Gentamicin<br>*T. maroccanus & roussonetii/P*ristinamycin<br>*T. maroccanus & broussonetii*/Cefixime | EC,Ss, KP, VC,PA, BS,BC, ML,SA | Checker-board | Synergistic | [58] |
| *Lippia sidoides*/ Thymol | SA, PA | Gaseous contact | Synergistic | [118] |
| *Coriandrum sativum*/Cefoperazone, *Coriandrum sativum/*Chloramphenicol<br>*Coriandrum sativum/*Ciprofloxacin<br>*Coriandrum sativum*/Gentamicin<br>*Coriandrum sativum*/Tetracycline<br>*Coriandrum sativum*/Piperacillin | AB | Micro-dilution | Synergistic | [119] |
| *Hymus vulgaris*/Methanol extracts<br>*Pimpinella anisum/*Methanol extracts | SA, BC, EC, PV, PM, ST, KP, PA | Broth micro-dilution | Synergistic | [120] |
| *Myrtus communis*/Polymixin B<br>*Myrtus communis/*Ciprofloxacine | AB | Checker-board | Synergistic | [121] |
| *Thymus vulgaris/Cinnamomum cassia* | AF | Micro-dilution | Partial synergistic | [122] |
| Cinnamon/Vanillin<br>Clove/Vanillin | LM, EC | Broth dilution | Synergistic | [123] |
| *Mentha piperita*/Sliver ion | EC, SA, CA | Checker-board | Synergistic | [124] |
| *Agastache rugosa*/Ketoconazole | BLC | Micro-dilution, Disk- diffusion Checker-board | Synergistic | [87] |
| *Coriandrum sativum*/Amphotericin B | CA, CT | Checker-board | Synergistic | [125] |
| *Peucedanum officinale/*Tetracycline<br>*Peucedanum officinale/*Treptomycin<br>*Peucedanum officinale/*Chloramphenicol | EC, KP, PM, PA, SA | Micro-dillution checker-board | Synergistic | [126] |
| *Boswellia Sacra/Nigella Sativa* | SA, PA, KP, SPT, EFA | Micro-dillution | Synergistic | [127] |
| *Cymbopogon citrates/ Cymbopogon giganteus* | EC, EA, EFA, LM, PA, SAN, ST, SD, SA | Checker-board | Synergistic, Additive and Indifferent | [128] |
| *Pelargomium graveolens/*Amphotericin B<br>*Origanum vulgare/*Amphotericin B | CA | Micro-dillution | Synergistic | [129] |

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|---|---|---|---|---|
| *Melaleuca alternifolia*/Amphotericin B | | | | |
| *Thymus maroccanus*/Amphotericin B<br>*Thymus maroccanus*/Fluconazol<br>*Thymus broussonetii*/Amphotericin B<br>*Thymus broussonetii*/Fluconazol | CA | Checker-board | Synergistic | [130] |
| *Eucalyptus globules*/Gentamicin | PA | Micro-dillution | Synergistic | [131] |
| *Tetraclinis articlata/Amoxicilline* | LM, SA, SAN, EC,KP, PA | Micro-dillution | Synergistic | [132] |
| *Myrtus communis/Thymus vulgaris* | SA, EC | Micro-dillution | Synergistic | [133] |
| *Origanum vulgare/Rosmarinus officinalis* | EC, LM, SAN, SEt, | Viable cell counts | Synergistic | [134] |
| *Rosa damascene/Lavandula angustifolia*<br>*Origanum heracleoticum/Lavandula angustifolia*<br>*Thymus vulgaris/Origanum heracleoticum* | AF, AA, FS, FSp, FE, FSo, FSe, Ps | Micro-dilution | Synergistic | [135] |

**Microorganisms:** *Alternaria alternata* (AA), *Acinetobacter baumannii* (AB), *Aggregatibacter actinomycetemcomitans* (AC), *Aspergillus flavus* (AF), *Aspergillus fumigates* (AFu), *Alternaria humicola* (AH), *Aspergillus niger* (AN), *Aspergillus oryzae* (AO), *Aspergillu sflavus* (AS), *Aspergillus sydowi* (ASy), *Aspergillus terreus* (AT), *Bacillus cereus* (BC), *Blastoschyzomyces capitatus (BLC), Brenneria nigrifluens* (BN), *Bacillus subtilis* (BS), *Candida albicans* (CA), *Cladosporium spp.* (Cs), *Citrobacter freundii* (CF), *Colletotrichum gloeosporioides* (CG), *Candida krusei* (CK), *Curvularia lunata* (CL), *Cryptococcus neoformans* (CN), *Corynebacterium rubrum* (CR), *Candida tropicalis* (CT), *Debaryomyces hansenii* (DH), *Enterobacter aregens* (EA), *Escherichia coli* (EC), *Enterococcus durans* (ED), *Enterococcus faecalis* (EFA), *Epidermophyton floccosum* (EF), *Eurotium sp.* (ES), *Enterobacter spp.* (ENs), *Fusarium subglutinans* (FS), *Fusarium sporotrichioides* (FSp), *Fusarium equiseti* (FE), *Fusarium oxysporum* (FO), *Fusarium solani* (FSo), *Fusarium semitectum* (FSe), *Fusarium nivale* (FN), *Klebsiella pneumoniae* (KP), *Kiebsiella spp.* (Ks), *Listeria innocua* (LI), *Listeria monocytogenes* (LM), *Microsporum canis* (MC), *Micrococcus flavus* (MF), *Micrococcus luteus* (ML), *Mycobacterium smegmatis* (MS), *Mucor plumbeus* (MP), *Methicillin resistant Staphylococcus aureus* (MRSA), *Pseudomonas aeruginosa* (PA), *Pseudomonas spp.*(Ps), *Pantoea agglomerans* (PAG), *Pectobacterium cartovorum* (PC), *Phytophthora cactorum* (PPC), *Porphyromonas gingivalis* (PG), *Pediococcus halophilus* (PH), *Penicillium italicum* (PI), *Penicillium spp. (*Ps), *Proteus mirabilis* (PM), *Penicillium notatum* (PN), *Penicillium roqueforti* (PR), *Proteus subtilis* (PS), *Proteus spp* (PRs), *Pseudomonas testosterone* (PT), *Rhizobium radiobacter* (RR), *Ralstonia solanacearum* (RS), *Rhizoctonia solani* (RSO), *Rhizobium vitis* (RV), *Rhizopus stolonifer* (RF), *Proteus vulgaris* (PV), *Staphylococcus aureus* (SA), *Saccharomyces cerevisiae* (SC), *Shigella dysenteriae* (SD), *Streptococcus faecium* (SF), *Staphylococcus epidermidis* (SE), *Salmonella enteritidis* (SE1), *Salmonella enteric* (SE2), *Streptococcus mutans* (SM), *Salmonella enteric* (SAN), *Streptococcus pyogenes* (SP), *Salmonella typhi* (ST), *Salmonella spp.*(SLs) *Salmonella paratyphi* (SPT), *Salmonella indica* (SI), *Streptococcus pneumoniae* (SP), *Shigella dysenteriae* (SD), *Serovar Enteritidis* (SEt), *Shigella sonnei* (SS), *Streptomyces scabies* (SSC), *Trichophyton mentagrophytes (TM), Trichophyton tonsurans* (TT), *Trichophyton rubrum* (TR), *Vibrio cholera* (VC), *Xanthomonas campestris* (XC), *Yersinia enterocolitica* (YE), *Zygosaccharomyces rouxii* (ZR).

## 6. Conclusion

Finally it can be concluded from the review that essential oils and their combination with antibiotics/ plant extracts can be used as novel antimicrobial agents against multidrug resistance pathogenic microorganisms**.** This combination may reduce antibiotic minimum effective dose and thus can minimize potential antibiotic side effects and prevent the emergence of antibiotic resistance. Despite the promising results given by *in vitro* studies there is still need to find molecular basis of mode of action of essential oils, chemical composition of oil and isolation of active constituent from oil.

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