Chapter 12
Antibacterial and Antifungal Activity of Secondary Metabolites of *Teucrium* Species

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Abstract *Teucrium* species are known for their medicinal properties and have exhibited different biological activities including broad-spectrum antimicrobial activity. Considering that *Teucrium* species produce various bioactive compounds (phenolic acids, flavonoids, saponines, alkaloids, monoterpenes, neo-clerodane diterpenes, sesquiterpenes, essential oils) they could be an important source of new antimicrobial compounds. The expanding of knowledge on the antimicrobial plant compounds has opened wide opportunities for their application in medicine, pharmacy, and food industry. Accordingly, the aim of this chapter was to collect and summarize the results of antimicrobial (antibacterial and antifungal) studies. The results for 44 *Teucrium* species were processed including both the activity of different types of plant extracts and essential oils. Antimicrobial properties were based on in vitro determination of zones of growth inhibition and minimal inhibitory concentrations, using diffusion and dilution method. *Teucrium* species established broad-spectrum antimicrobial activity. Generally, the species were more active against Gram-positive than Gram-negative bacteria and fungi. The essential oils were more potent than plant extracts. The following *Teucrium* species exhibited a promising antimicrobial activity: plant extracts of *Teucrium flavum*, *T. fruticans*, *T. siculum*, *T. yemense*, *T. sokotranum*, *T. persicum* and *T. scordium*, especially against Gram-positive bacteria, and essential oils from *Teucrium orientale*, *T. africanum*, *T. ramosissimum*, *T. mascatence*, *T. yemense*, *T. massiliense* and *T. scordonia*. *Teucrium polium* was one of the most tested *Teucrium* species and has exhibited pronounced activity. The activity was observed against important pathogenic bacteria (*Staphylococcus* sp., *Bacillus* sp., *Enterococcus* sp., *Streptococcus* sp., *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Salmonella* sp.) and fungi (*Candida* sp., *Trychophyton* sp.). In the last 20 years, the significant database of antimicrobial properties of *Teucrium* species is formed. However, the mechanisms of activity are still poorly explored. Only with exact knowledge of these mecha-

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nisms, it will be possible to develop a new generation of standardized, effective biopreparations. Future studies on bioavailability, pharmacodynamics, and mechanisms of action will contribute to the development of new *Teucrium* antimicrobial agents.

Keywords *Teucrium* · Plant extracts · Essential oils · Bacteria · Fungi · Antibacterial effects · Antifungal effects

Abbreviations

AcOH	Acetone
BuOH	Buthanol
CFU	Colony forming unit
$CHCl_3$	Chloroform
conc.	Concentration
DIZ	Diameter of inhibition zone
DMC	Dihlormethane
EtAc	Ethyl acetate
EtOH	Ethanol
G^-	Gram-negative bacteria
G^+	Gram-positive bacteria
Hex.	Hexane
MDR	Multi-drug resistant
MeOH	Methanol
MIC	Minimal inhibitory concentrations
MRSA	Methicillin-resistant *Staphylococcus aureus*
RPMI	Roswell Park Memorial Institute
TLC	Thin layer chromatography

12.1 Introduction

Various medicinal plants were, for a long time, used for infectious diseases healing. Medicinal plants synthesized different volatile and non-volatile compounds which exhibit inhibitory effects on growth and division of pathogenic microorganisms. Essential oils, balsams, resins of many aromatic plants (exp. *Salvia officinalis*, *Matricaria chamomilla*, *Eucalyptus globulus*, *Syzygium aromaticum*, *Myrtus communis*) are used as remedies for oral hygiene, tooth decay and gingivitis, wound healing. The essential oils of *Thymus vulgaris*, *T. serphyllum*, *Origanum vulgare*, *Ocimum basilicum* content thymol and carvacrol, compounds which interrupt the growth of microorganisms. *Melaleuca alternifolia* essential oil is a common

therapeutic agent to treat acne and other skin infectious problems. The well-known aromatic plants with the antimicrobial property are *Allium sativum*, *A. cepa* and other species of *Allium* genus which by hydrolysis of glycosides realized volatile sulfur-containing bioactive compounds. Antimicrobial activity possesses and numerous nonvolatile plant's compounds efficient for wound healing, infection, and inflammation of mucous membrane of the digestive tract, digestive disorders, and diarrhea. Proanthocyanidins from *Vaccinium macrocarpon* are used to treat urinary tract infections. Moreover, the plant- and spice-based antimicrobial compounds derived from *Cinnamomum* sp., *Syzygium aromaticum*, *Sinapsis alba*, *Laurus nobilis*, *Carum carvi*, *Coriandrum sativum*, *Cuminum cyminum*, *Origanum vulgare*, *Rosmarinus officinalis* and *Salvia officinalis* are used as natural preservatives for food preservation and food safety (Stefanović et al. 2009, 2012; Tajkarimi et al. 2010; Saleem et al. 2010; Ličina et al. 2013; Antolak and Kregiel 2017; Ionescu 2018).

The healing properties of species from genus *Teucrium* (family Lamiaceae) are well-known. In traditional medicine, the most common uses of these plants are as a diuretic, diaphoretic, tonic, analgesic, antipyretic, antirheumatic and antiseptic agent. In the Serbian herbal medicine, *Teucrium* species (*Teucrium chamaedrys*, *T. montanum*, *T. polium* and *T. scordium*) are used as a tonic, antirheumatic, digestion stimulant as well as an antiseptic agent (Sarić 1989). In recent years, numerous studies on *Teucrium* species bioactivities including antispasmodic, anti-inflammatory, antihypertensive, hypoglycemic, anticancer, antimicrobial and antioxidant, were reported. The expanding of knowledge on the antimicrobial plant compounds has opened wide opportunities for their application in both the medical and cosmetic purposes, and, also, in the food industry for storing and preserving food products. Accordingly, the goal of this chapter was an up-to-date literature review on antimicrobial activity of *Teucrium* species summarizing the results and selecting the most potent species for further potential application.

12.2 Bioactive Plant Compounds

Medicinal and prophylactic properties of medicinal plants are attributed to the synthesized bioactive organic compounds, the products of secondary metabolism of plants. The one of widely accepted classification of secondary metabolites is into three large classes: phenolic compounds (8000 types), terpenes (25,000 types), and alkaloids (12,000 types) (Antolak and Kregiel 2017).

The phenolic compounds are one of the largest groups of secondary metabolites that have exhibited antimicrobial activity. Important subclasses in this group of compounds include phenols, phenolic acids, quinones, flavonoids, tannins, and coumarins. Phenols are a class of chemical compounds consisting of a hydroxyl functional group (-OH) attached to an aromatic phenolic group. The site(s) and the number of hydroxyl groups on the phenol group are thought to be related to their

relative toxicity (Cowan 1999). Quinones have aromatic rings with two ketone substitutions. Quinones have the potential to form an irreversible complex with nucleophilic amino acids in proteins (Cowan 1999). Flavonoids are also hydroxylated phenolic substances but occur as a C6-C3 unit linked to an aromatic ring. They are classified according to their biosynthetic origin into the following classes: flavones, flavonols, flavanones, flavanols, anthocyanidins, isoflavones (Cowan 1999; Cushnie and Lamb 2011). Hydrolyzable and condensed tannins are found in almost every plant part: bark, wood, leaves, fruits, and roots. Hydrolyzable tannins are polyesters of gallic acid (or its derivatives), and the sugar. The condensed tannins are formed by the coupling of flavan-3-ol or flavan-3,4-diol monomers. Coumarins are benzo-α-pyrones and could be categorized as simple coumarins and cyclic coumarins (furanocoumarins and pyranocoumarins) (Ojala 2001).

Terpenes are organic compounds built up from isoprene subunits. According to the number of isoprene subunits, there are monoterpenes (C10), sesquiterpenes (C15), diterpenes (C20), triterpenes (C30), tetraterpenes (C40) and polyterpenes. Monoterpenes, diterpenes, and sesquiterpenes are the primary constituents of the essential oils (Kovačević 2004).

Alkaloids, one of the earliest isolated bioactive compounds from plants, are divided into the three classes: true alkaloids – heterocyclic nitrogen compounds derived from amino acids, protoalkaloidis – derived from amino acids, but not contain nitrogen in a heterocyclic ring and pseudoalkaloids – not derived from amino acids (Kovačević 2004).

12.3 Mechanisms of Antimicrobial Activity of Plant Compounds

The antimicrobial efficiency of plant compounds depends on several factors: (i) characteristics of target microorganism (the type, genus, species, strain), (ii) characteristics of plant material (botanical source, composition of the bioactive compounds as well as time of harvesting, stage of development or method of extraction) and (iii) chemical properties (hydrophilicity, lipophilicity, concentration, pH value).

The antibacterial activity occurs through several mechanisms: (i) disruption of membrane structure and function (including the efflux system), (ii) interruption of DNA/RNA synthesis and function, (iii) interference with intermediary metabolism, (iv) induction of coagulation of cytoplasmic constituents (Cowan 1999; Kovačević 2004; Buzzini et al. 2008; Cushnie and Lamb 2011; Daglia 2012; Radulović et al. 2013; Coppo and Marchese 2014). The mechanisms of antibacterial action for the particular class of bioactive compounds are summarized in Table 12.1.

In addition, plant compounds are being able to suppress bacterial toxin production by reducing the expression of major virulence genes. Selected plant extracts inhibit the production of cholera toxin by *Vibrio cholerae*, reduce the production of *Staphylococcus aureus* α-hemolysin, enterotoxins and toxic shock syndrome toxin

Table 12.1 Mechanisms of antibacterial activity of plant compounds

Class of plant compounds	Mechanism of action
Phenols	Changing the permeability of cell membrane and causing the leakage of cellular content, interfere with membrane proteins resulting in structure disrupting
Flavonoids	Cell membrane disruption, inhibition of nucleic acid synthesis (caused by topoisomerase inhibition), inhibition of energy metabolism (caused by NADH-cytochrome c reductase or ATP synthase inhibition), disturbance of cell wall and cell membrane synthesis
Quinones	Formation of irreversible complex with surface-exposed adhesins, cell wall polypeptides, and membrane-bound enzymes
Proanthocyanidins	Destabilization of cell membrane, inhibition of extracellular microbial enzymes, direct actions on microbial metabolism, deprivation of the substrates required for microbial growth
Gallotannins	Inactivation of membrane-bound proteins, strong affinity for iron
Coumarins	Decrease cell respiration
Essential oils	Cell membrane disruption
Alkaloids	Intercalate with DNA, inhibition of enzymes (esterase, DNA- polymerase, RNA-polymerase) or cell respiration

1, reduce the production of vero toxin and inactivate Shiga toxins (Upadhyay et al. 2014). Moreover, it was observed that plant extracts and essential oils inhibit bacterial biofilm formation, motility, attachment, and cell communication (Huber et al. 2003; Borges et al. 2015; Stefanović et al. 2015; Muruzović et al. 2016; Silva et al. 2016). Biofilm is defined as a structured community of bacterial cells enclosed in a self-produced polymeric matrix and adherent to an inert or living surface (Hall-Stoodley et al. 2004). The ability to form biofilm is recognized as an additional virulence factor which contributes to the long-lasting persistence of bacterium. In biofilms, bacteria show great tolerance toward antibacterial agents and host immune defenses what makes difficulties in control and eradication of bacterial infections (Høiby et al. 2010).

Studies investigating the mechanism of antifungal activity showed that plant compounds (essential oils, plant extracts) demonstrate several negative effects on fungal cell: (i) cause changes in cell membrane function or structure and, also, in the membranes of organelles (ii) inhibit key enzymes in normal physiological metabolism (respiration and energy production), (iii) inhibit the synthesis of the main polymers of the fungal cell wall, (iv) induce differential expression of critical genes including those involved in the cellular drug response, oxidation-reduction processes, pathogenesis, and the cellular starvation response (Carson et al. 2006; Li et al. 2013, 2014, 2016).

12.4 Extraction of Plant Compounds

Medicinal plants may have been specifically cultivated or collected from the wild. After harvesting, plant material should be cleaned, sorted, and then subjected to extraction. Fresh or dried plant material can be used. Extraction and isolation of the bioactive compounds from the plant tissues can be performed by using different procedures and methods (solvent extraction, distillation, supercritical fluid extraction). The appropriated extraction procedure used depends on the physical and chemical properties of the plant material, texture, water content in plant material, as well as the nature and kind of the compound to be isolated.

Solvent extraction is a process of separation of active compounds from plant material using different solvents. During extraction, solvents diffuse into the plant tissues and solubilise compounds with similar polarity. After the extraction process has finished, solvents have been evaporated, so that an extract is a concentrated mixture of plant active compounds. Successful extraction is largely dependent on the type of solvent used in the extraction procedure. The desirable properties of extracting solvents are: selectivity, large extraction capacity, no interference with plant components, no toxicity, and high evaporation level. The most often tested extracts are: water extract as a sample of extract that primarily used in traditional medicine and extracts from organic solvents such as methanol, ethanol as well as ethyl acetate, acetone, chloroform, dichlormethane (Ncube et al. 2008).

Distillation is a process of separation of volatile active compounds from plant material by physical process of evaporation, treating plant material with steam or boiling. After cooling and condensation of vaporized compounds, the water distillate is formed. Due to essential oils are insoluble in the water and because of specific gravity, essential oils are separated at the surface or top of the water distillate and further collected. Essential oils are extracted by steam distillation or hydrodistillation (Tongnuanchan and Benjakul 2014).

Supercritical fluid extraction is a diffusion-based process of separation of plant active compounds using supercritical fluids as the extracting solvent. Supercritical fluids are formed by heating of gases above their critical temperatures or by compressing of liquids above their critical pressure. Carbon dioxide is the most used supercritical fluid. Supercritical fluids have dissolving properties that depend on their density and can be controlled with temperature and pressure. In relation to solvent extraction, supercritical fluid extraction has some advantages such as low extraction temperature, minimal degradation of the active substances, selectively dissolving of compounds, and faster extraction (Janaćković et al. 2017).

12.5 Antimicrobial Susceptibility Methods

Antimicrobial (antibacterial and antifungal) activity of plant extracts, essential oils, and pure compounds might be analysed using several methods: diffusion, dilution and bioautography method (Fig. 12.1). Diffusion and dilution method are frequently

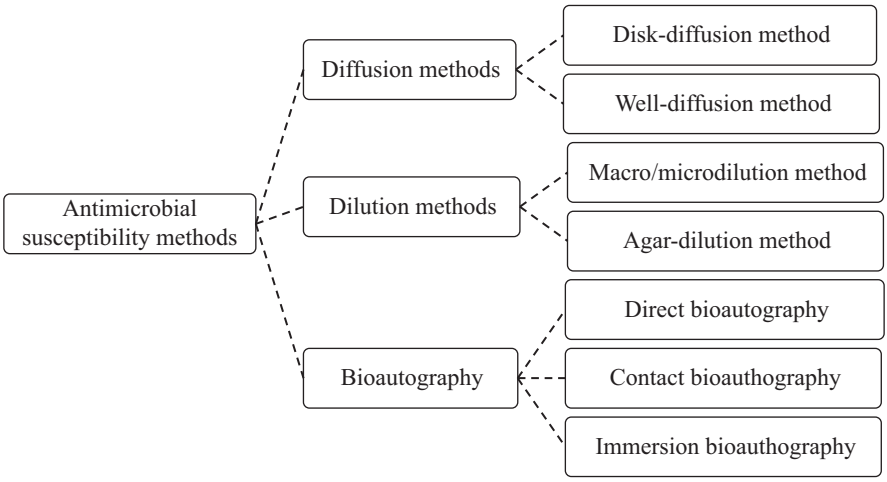

Fig. 12.1 Classification of antimicrobial susceptibility methods

used. These methods are standard antimicrobial susceptibility testing methods used for antibiotics/antifungal drugs recommended by the Clinical and Laboratory Standards Institute, USA.

Diffusion method is a qualitative test which, according to a size of a diameter of the zone of growth inhibition, shows the intensity of antimicrobial effect of the tested compound and allows classification of microorganisms as susceptible or resistant. The tested compound has applied on disk or into a hole in agar medium inoculated with a microorganism to be tested. During incubation, the compound diffuses into the medium inhibiting the growth of a microorganism. The reference medium for testing is Mueller-Hinton agar for bacteria and Mueller-Hinton agar supplemented with 2% glucose for fungi. The density of inoculum should be equivalent to 0.5 McFarland standard ($1–2 \times 10^8$ CFU/ml). The results are recorded as zones of growth inhibition and when the diameter of the inhibition zone is wider, the antimicrobial activity of the compounds is higher (Fig. 12.2). The rate of diffusion of the tested compounds through the agar is dependent on solubility properties and the molecular weight of the tested compound. Hence, this method is not suitable to natural antimicrobial compounds that are scarcely soluble or insoluble in water and thus their hydrophobic nature prevents uniform diffusion through the agar medium (Klancnik et al. 2010).

Dilution (macrodilution and microdilution) method is more appropriate when investigating the activity of plant products. It can be carried out by using test tubes (macrodilution) or 96-wells microtiter plates (microdilution). The serial twofold dilutions of a tested compound are prepared in a liquid medium, Mueller-Hinton broth for bacteria and RPMI 1640 broth for fungi. The density of final inoculum is 5×10^5 CFU/ml for bacteria and $5 \times 10^2 – 2.5 \times 10^3$ cell/ml for yeasts. This method is quantitative, the activity of a compound or a plant extract is determined as minimal inhibitory concentration (MIC). MIC is defined as the lowest concentration of

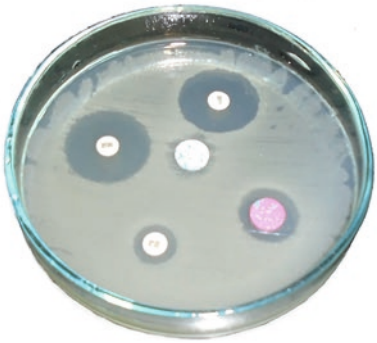

Fig. 12.2 Diffusion method – the zones of growth inhibition around disks indicate the activity of tested compound

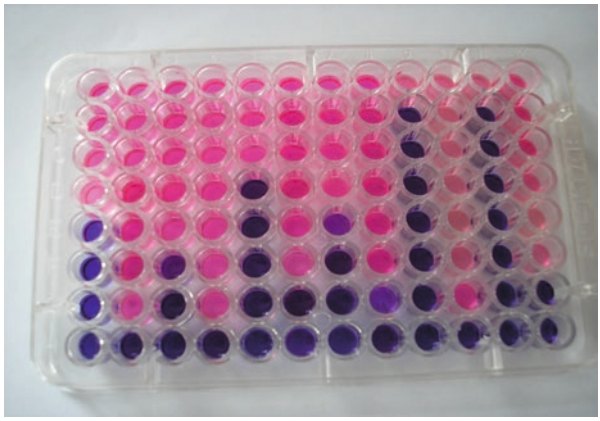

Fig. 12.3 Microdilution method – the change of colour of indicator (resazurine) from blue to pink indicates the growth of bacteria

tested compound able to inhibit the visible growth of microorganisms. Microbial growth (growth of bacteria and yeasts) could be assessed either visually by grading turbidity or spectrophotometrically by measuring optical density. Moreover, easy MIC detection and increased credibility of this method allow using of growth indicators which changing the colour indicate the growth of microorganisms (Cos et al. 2006; Fig. 12.3).

Once more method used for determination of MIC is agar dilution method. In this method, dilutions of a plant extract or a compound are prepared by adding into a precise volume of molten agar medium which then poured into sterile petri plates. Each agar plate containing a different concentration of tested compound. MIC is recorded as the lowest concentration of the compound that completely inhibits the growth, no colony observed.

Bioautography rely on fractionalisation of the extracts on its different components simplifies the identification of compounds with antimicrobial potency. Bioautography may be direct, when microorganisms grow directly on a TLC plate, then contact, when the active compound is transferred from a TLC plate to inoculated agar, and immersion when the inoculated agar medium is spilled over a TLC plate. Clear (white) zones on the TLC plate indicate antimicrobial activity of the extracts and their components (Rahalison et al. 1991).

12.6 Antimicrobial Activity of *Teucrium* Species

Antibacterial and antifungal activity of *Teucrium* species has been extensively investigated. In the following sections, the results of the literature search of databases Scopus, PubMed, Google Scholar for period 1999–2019 (the last accessed was on April 1, 2019) were presented. According to published data, 16% of species of the genus *Teucrium* (total of 44 species) were screened for antimicrobial testing. The genus *Teucrium* includes 268 species. The species from different regions (Serbia, Croatia, Italy, Romania, Turkey, Pakistan, Jordan Iran, Tunisia, Algeria, Mexico) were investigated, so the results were summarised and compared.

Evidently, bioactive compounds from *Teucrium* species were frequently isolated in a form of plant extracts. Plant extracts were prepared from fresh or dried plant material using conventional extraction methods (Soxhlet extraction, maceration, decoction) and most recent supercritical fluid extraction. The most commonly used extracting solvents were methanol, ethanol, and water. The more detailed information on plant parts used or extraction procedure and solvents used are presented in Table 12.2.

The essential oils were isolated by hydrodistillation or steam distillation using a Clevenger-type apparatus. A total of 20 *Teucrium* species essential oils were analysed and screened for antimicrobial activity (Table 12.3). For the most part, antimicrobial activity was determined using diffusion or dilution method. However, activity has also been demonstrated using time-kill assays. Antimicrobial activity studies were carried out on numerous bacterial species (Gram-positive and Gram-negative strains; sensitive and resistant, pathogens and opportunistic pathogens, clinical isolates and standard strains) and fungal species (yeasts, dermatophytes, and filamentous fungi, human and phytopathogens, clinical isolates and standard strains).

Teucrium species exhibited broad-spectrum antimicrobial activity (Fig. 12.4). Mostly, antimicrobial properties of *Teucrium* species were based on their activity against planktonic bacteria (bacteria in suspensions). In most environments, bacteria form biofilms, surface-attached communities. Many chronic infections (urinary tract infections, middle-ear infections, tooth decay and paradontosis, prostheses-associated infection) or problems with contamination in food processing industry are being connected with biofilms (Costerton et al. 1999; Wood et al. 2011). So, in recent years, the investigation of new active plant-derived antibiofilm agents is

Table 12.2 List of different plant extracts, plant part used, tested microorganisms, and results of *Teucrium* species antimicrobial activity

Teucrium species (part used)	Type of extract (extraction method)	Tested microorganisms	DIZ (tested concentration) range, MIC range		References
			Antibacterial activity	Antifungal activity	
T. polium (flowers) Iran	Ethanol extract (Maceration)	489 isolates of *Staphylococcus aureus*	DIZ (30 mg/ml) 10–11 mm	Not tested	Mansouri (1999)
T. polium (aerial parts) Turkey	Ethanol extract (Soxhlet)	*Listeria monocytogenes*, *L. ivanovii*, *L. innocua*, *L. murrayi*	DIZ (133 mg/ml) 10–11 mm MIC 12.5–50μg/ml	Not tested	Altanlar et al. (2006)
T. polium (aerial parts) Jordan	Ethanol extract (Maceration)	*S. aureus*, *Pseudomonas aeruginosa*, *Candida albicans*	DIZ (80 ppm) 14–15 mm MIC 80 ppm	Not active	Khalil et al. (2009)
T. polium (aerial parts) Jordan	Methanol extract (Soxhlet)	*Escherichia coli* ATCC 25922, *P. aeruginosa* ATCC 27853, *Proteus mirabilis* ATCC 426, *Enterobacter cloaceae* ATCC 29004, *S. aureus* ATCC 25923	DIZ (10 mg/ml) 11–26 mm MIC 1.2–2.4 mg/ml	Not tested	Tarawneh et al. (2010)
T. polium (aerial parts) Iran	Ethanol, methanol extracts (Maceration)	*Brucella melitensis*	DIZ_{EtOH} (100–400μg/ml) 9–12 mm DIZ_{MeOH} (100–400μg/ml) 8–11 mm	Not tested	Motamedi et al. (2010)
T. polium (aerial parts) Iran	Ethanol, methanol extracts (Maceration)	*Bacillus pumilis*, *B. anthracis*, *B. licheniformis*, *B. cereus*, *S. aureus*, *S. epidermidis*, *E. coli*, *Yersinia enterocolitica*, *S. typhy*, *P. mirabilis*, *Bordetella bronchispetica*, *Streptococcus pyogenes*	DIZ_{EtOH} (400 mg/ml) 9–18 mm DIZ_{MeOH} (600 mg/ml) 9–26 mm	Not tested	Darabpour et al. (2010)

T. polium (aerial parts) Egypt	Ethanol, ethyl acetate, chloroform, n-hexane extracts (Maceration)	*Trichophyton rubrum*, *T. tonsurans*, *C. albicans*, *Chrysosporium tropicum*, *Paecilomyces lilacinus*, *P. variotii*, *Scopulariopsis bervicaulis*	Not tested	MIC_{EtOH} 75– > 150 mg/ml MIC_{EtAc} 75– > 150 mg/ml MIC_{CHCl3} 25–125 mg/ml $MIC_{Hex.}$ 25– > 150 mg/ml	Hashem (2011)
T. polium (aerial parts) Turkey	Water extract (Maceration)	*Klebsiella pneumoniae*, *Haemophilus influenzae* ATCC 49766, *P. aeruginosa* ATCC 10145, *Acinetobacter baumannii*, *Streptococcus pneumonia* ATCC 19615, *S. pyogenes* ATCC 13615, *S. aureus* ATCC 25923, *S. epidermidis* ATCC 12228, *Mycobacterium tuberculosis*, *C. albicans* ATCC 10231, *C. parapsilosis* ATCC 22019, *C. krusei*, *C. tropicalis*	MIC 64µg/ml (G^+ bacteria) MIC 16–32µg/ml (G^- bacteria)	MIC 8–64µg/ml	Deliorman Orhan et al. (2012)
T. polium (aerial parts) Serbia	Methanol, acetone, ethyl acetate extracts (Maceration)	*S. aureus* ATCC 25923, *S. aureus*, *E. coli* ATCC 25922, *E. coli*, *P. aeruginosa*, *C. albicans* ATCC 10231, *C. albicans*, *A. niger*	MIC_{MeOH} 0.3–20 mg/ml MIC_{AcOH} 0.3–20 mg/ml MIC_{EtAC} 0.3, 10 mg/ml (*S. aureus* ATCC 25923, *P. aeruginosa*)	MIC_{MeOH} > 20 mg/ml MIC_{AcOH} > 20 mg/ml MIC_{EtAC} > 10 mg/ml	Stanković et al. (2012)
T. polium (aerial parts) Iran	Ethanol extract (Maceration)	*S. typhi*, *P. aeruginosa*, *B. cereus*, *L. monocytogenes*, *S. aureus*	DIZ (50 mg/ml) 6–21 mm MIC 6.25–50 mg/ml	Not tested	Mirzaei et al. (2013)
T. polium (aerial parts) Palestine	Ethanol extract (Maceration)	*S. aureus* ATCC 29213, *B. subtilis* ATCC 6633, *M. luteus* ATCC 10240, *E. coli* ATCC 10536, *P. aeruginosa*, *K. pneumoniae*, *C. albicans* ATCC 10231, *A. niger* ATCC 16404	DIZ (25 mg/ml) 8.7–18.3 mm	DIZ (25 mg/ml) 19.7 mm (*C. albicans*)	Qabaha (2013)

(continued)

Table 12.2 (continued)

Teucrium species (part used)	Type of extract (extraction method)	Tested microorganisms	DIZ (tested concentration) range, MIC range		References
			Antibacterial activity	Antifungal activity	
T. polium (leaves) Algeria	Methanol extract (Maceration)	*E. coli* ATCC 25922, *S. aureus* ATCC 6538	DIZ (2 mg/ml) 14–15 mm MIC 13 mg/ml (*S. aureus*) MIC 13 mg/ml (*E. coli*)	Not tested	Khaled-Khodja et al. (2014)
T. polium (aerial parts) Algeria	Methanol extract (Maceration)	*S. aureus* ATCC 25923, *E. coli* ATCC 25922, *S. typhimurium* ATCC 10428, *P. aeruginosa* ATCC 27853, *E. faecalis* ATCC 29212, *K. pneumoniae* ATCC 700603, *B. subtilis* ATCC 7033	DIZ (600 mg/ml) 11.5–26 mm MIC 3.125–50 mg/ml	Not tested	Dridi et al. (2016)
T. polium subsp. *gabesianum* (aerial parts) Tunisia	Ethanol, water extracts (Maceration)	*E. coli* ATCC 25922, *E. faecalis* ATCC 29212, *S. aureus* ATCC 25923, *P. aeruginosa* ATCC 27853, *C. freundeii*, *P. mirabilis*, *C. albicans*, *Cryptococcus neoformans*, *Trichophyton rubrum*, *T. soudanense*, *Microsporum canis*, *A. fumigatus*, *Scopulariopsis brevicaulis*	MIC_{EtOH} 0.156–0.625 mg/ml MIC_{H2O} 0.156–0.625 mg/ml	MIC_{EtOH} 0.625– > 1 mg/ml MIC_{H2O} > 1 mg/ml	Ben Othman et al. (2017)
T. polium (aerial parts) Pakistan	Ethanol, ethyl acetate, dichloromethane acetone, hexane extracts (Maceration)	*E. coli* ATCC 15224, *B. subtilis* ATCC 6663, *S. aureus* ATCC 29213, *S. flexneri* ATCC 14028, *A. flavus* ATCC 32611, *A. niger*, *C. albicans* ATCC 2091, *T. longifusus*	EtOH (1 mg/ml) 37–73% of inhibition EtAc (1 mg/ml) 24–56% DCM (1 mg/ml) 25–37% AcOH (1 mg/ml) 30–31% Hex. (1 mg/ml) 10–35%	EtOH (1 mg/ml) 40–70% of inhibition EtAc (1 mg/ml) 10–65% DCM (1 mg/ml) 27–58% AcOH (1 mg/ml) 15–25% Hex. (1 mg/ml) 25–30%	Ali et al. (2018)

T. polium (leaves, flowers, stem) Turkey	Ethanol, acetone, ether extracts (Maceration)	*B. subtilis* NRRL 558, *B. cereus* NRRL 3711, *S. aureus* NRRL 767, *S. epidermidis* NRRL 4377, *S. lutea* NRRL 4370, *E. coli* NRRL 3008, *E. aerogenes* NRRL 3567, *S. typhimurium* NRRL 4420, *Shigella* sp., *C. albicans* NRRL 27077, *Pichia membranifaciens* NRRL 2026, *S. cerevisiae* NRRL 2034, *Shizosaccharomyces pombe* NRRL 12796, *Zygosaccharomyces rouxii* NRRL 229	DIZ (1 mg/ml) 8–14 mm (G^+ bacteria) DIZ (1 mg/ml) 8–9 mm (G^- bacteria)	DIZ (1 mg/ml) 8–18 mm	Kunduhoglu et al. (2011)
T. chamaedrys subsp. *chamaedrys* (flowers) Turkey			DIZ (1 mg/ml) 8–22 mm (G^+ bacteria) DIZ (1 mg/ml) 8–13 mm (G^- bacteria)	DIZ (1 mg/ml) 8 mm	
T. chamaedrys Turkey	Polar and non-polar fractions of methanol extract (Soxhlet)	*S. pneumoniae*, *B. cereus*, *Acinetobacter lwoffii* ATCC 19002, *E. coli*, *K. pneumoniae*, *Clostridium perfringens*, *C. albicans*, *C. krusei* ATCC 6258	MIC_{polar} > 72 mg/ml $MIC_{non\text{-}polar}$ 9– > 72 mg/ml	MIC_{polar} > 72 mg/ml MIC_{non^-polar} 18–36 mg/ml	Gursoy and Tepe (2009)
T. chamaedrys (aerial parts) Turkey	Water, ethanol, ethyl acetate, hexane extracts (Maceration)	*B. cereus*, *S. aureus* ATCC 6538P, *E. coli* O157:H7, *K. pneumoniae*, *C. albicans* ATCC 10239, *S. aureus* ATCC 49444, *L. monocytogenes* ATCC 13076, *E. coli* ATCC 25922, *S. typhymurium* ATCC 14028, *C. albicans* ATCC 10231	MIC_{H2O} 12.5–150 mg/ml MIC_{EtOH} 400 mg/ml (G^+ bacteria) MIC_{EtAC} 3.12–12.5 mg/ml $MIC_{Hex.}$ – not active MIC (*S. aureus*) 3.12 mg/ml	MIC_{EtAC} 400 mg/ml	Ceyhan et al. (2012)
T. chamaedrys (aerial parts) Serbia	Methanol, acetone, ethyl acetate extracts (Maceration)	*S. aureus* ATCC 25923, *E. coli* ATCC 25922, *S. aureus*, *E. coli*, *P. aeruginosa*, *C. albicans* ATCC 10231, *C. albicans*, *A. niger*	MIC_{MeOH} 0.078–5 mg/ml MIC_{AcOH} 5– > 20 mg/ml MIC_{EtAC} 0.6– > 10 mg/ml	MIC_{MeOH} > 20 mg/ml MIC_{AcOH} 10 mg/ml (*A. niger*) MIC_{EtAC} 10 mg/ml (*A. niger*)	Stanković et al. (2012)

(continued)

Table 12.2 (continued)

Teucrium species (part used)	Type of extract (extraction method)	Tested microorganisms	DIZ (tested concentration) range, MIC range		References
			Antibacterial activity	Antifungal activity	
T. chamaedrys (aerial parts) Romania	Ethanol extract (Maceration)	*S. aureus* ATCC 49444, *L. monocytogenes* ATCC 13076, *E. coli* ATCC 25922, *S. typhimurium* ATCC 14028, *C. albicans* ATCC 10231	DIZ 11–20 mm	DIZ 22 mm	Vlase et al. (2014)
T. chamaedrys (aerial parts) Serbia	Water extract (Supercritical water extraction)	*S. aureus* ATCC 25923, *E. coli* ATCC 25922, *B. subtilis* ATCC 6633, *P. vulgaris* ATCC 13315, *P. mirabilis* ATCC 14153, *K. pneumoniae* ATCC 13883, *C. albicans* ATCC 10231, *A. niger* ATCC 16404	MIC 78.125–312.5μg/ml	MIC 78.125–156.25μg/ml	Nastić et al. (2018)
T. montanum (aerial parts) Serbia	Petroleum ether, chloroform, ethyl acetate, n-butanol (Maceration)	*P. aeruginosa*, *E. coli*, *S. aureus*, *S. lutea*, *Bacillus* sp.	DIZ_{Ether} (10 mg/ml) 0 mm, MIC_{Ether}10– > 10 mg/ml DIZ_{CHCl3} (10 mg/ml) 15–18 mm, MIC_{CHCl3} 5–10 mg/ml DIZ_{EtAC} (10 mg/ml) 16–19.8 mm, MIC_{EtAC} 1– > 10 mg/ml $DIZ_{Butanol}$ (10 mg/ml) 16–20 mm, $MIC_{Butanol}$ 1– > 10 mg/ml	Not tested	Djilas et al. (2006)

T. montanum (aerial parts) Serbia	Methanol, acetone, ethyl acetate extracts (Maceration)	*S. aureus* ATCC 25923, *E. coli* ATCC 25922, *S. aureus*, *E. coli*, *P. aeruginosa*, *C. albicans* ATCC 10231, *C. albicans*, *A. niger*	MIC_{MeOH} 0.15–5 mg/ml MIC_{AcOH} 0.15–20 mg/ml MIC_{EtAC} 0.3, 10 mg/ml (*S. aureus* ATCC, *P. aeruginosa*)	MIC_{MeOH} > 20 mg/ml MIC_{AcOH} 20 mg/ml (*A. niger*) MIC_{EtAC} > 20 mg/ml	Stanković et al. (2012)
T. arduini (leaves, flowers) Croatia	Infusions	*B. subtilis* NCTC 8236, *S. aureus* ATCC 6538, *E. coli* ATCC 10535, *P. aeruginosa* ATCC 27853, *C. albicans* ATCC 10231, *A. niger* ATCC 16404	MIC_{leaves} 25–50 mg/ml (*B. subtilis*) MIC_{leaves} 1.56–4.16 mg/ml (*S. aureus*) $MIC_{flowers}$ 16.66 mg/ml (*S. aureus*)	Not active	Šamec et al. (2010)
T. arduini (aerial parts) Serbia	Methanol, acetone, ethyl acetate extracts (Maceration)	*S. aureus* ATCC 25923, *E. coli* ATCC 25922, *S. aureus*, *E. coli*, *P. aeruginosa*, *C. albicans* ATCC 10231, *C. albicans*, *A. niger*	MIC_{MeOH} 0.15–10 mg/ml MIC_{AcOH} 0.6– > 20 mg/ml MIC_{EtAC} 0.6– > 20 mg/ml	MIC_{MeOH} > 20 mg/ml MIC_{AcOH} > 20 mg/ml MIC_{EtAC} > 20 mg/ml	Stanković et al. (2012)
T. arduini (leaves, flowers, stem) Croatia	Ethanol extract (Ultrasonication)	*S. aureus* ATCC 6538, *E. faecalis* ATCC 21212, *E. coli* ATCC 10535, *P. aeruginosa* ATCC 27853, *C. albicans* ATCC 10231, *A. brasiliensis* ATCC 16404, *Microsporum gypseum*	MIC_{leaves} 2–4 mg/ml $MIC_{flowers}$ 2– > 4 mg/ml MIC_{stem} > 4 mg/ml	MIC_{leaves} 2– > 4 mg/ml $MIC_{flowers}$ 1– > 4 mg/ml MIC_{stem} 2– > 4 mg/ml	Kremer et al. (2013)

(continued)

Table 12.2 (continued)

Teucrium species (part used)	Type of extract (extraction method)	Tested microorganisms	DIZ (tested concentration) range, MIC range		References
			Antibacterial activity	Antifungal activity	
T. scordium subsp. *scordioides* (aerial parts) Serbia	Methanol, dichlormetan, cyclohexane extracts (Maceration)	*S. aureus* ATCC 25923, *S. epidermidis* ATCC 12228, *M. luteus* ATCC 10240, *E. faecalis* ATCC 29212, *B. subtilis* ATCC 6633BB, *B. cereus* ATCC 11778, *E. coli* ATCC 25922, *P. aeruginosa* ATCC 27853, *K. pneumoniae* NCIMB 9111, *C. albicans* ATCC 10259	DIZ_{MeOH} (100 mg/ml) 6.5 mm (*P. aeruginosa*) DIZ_{DCM} (100 mg/ml) 6–11 mm (*P. aeruginosa, B. subtilis*) $DIZ_{Hex.}$ (100 mg/ml) 6.5–11 mm	Not active	Kundaković et al. (2011)
T. scordium subsp. *scordium* Serbia	Methanol, acetone, ethyl acetate extracts (Maceration)	*S. aureus* ATCC 25923, *E. coli* ATCC 25922, *S. aureus*, *E. coli*, *P. aeruginosa*, *C. albicans* ATCC 10231, *C. albicans*, *A. niger*	MIC_{MeOH} 0.3–20 mg/ml MIC_{AcOH} 0.6– > 20 mg/ml MIC_{EtAC} 0.6, 10 mg/ml (*S. aureus* ATCC, *P. aeruginosa*)	MIC_{MeOH} > 20 mg/ml MIC_{AcOH} > 20 mg/ml MIC_{EtAC} 5–10 mg/ml	Stanković et al. (2012)
T. scordium subsp. *scordioides* (aerial parts) Serbia			MIC_{MeOH} 0.3–20 mg/ml MIC_{AcOH} 0.6 mg/ml (*S. aureus* ATCC) MIC_{EtAC} 0.6, 10 mg/ml (*S. aureus* ATCC, *P. aeruginosa*)	MIC_{MeOH} > 20 mg/ml MIC_{AcOH} > 20 mg/ml MIC_{EtAC} > 10 mg/ml	
T. stocksianum (whole plant) Pakistan	Methanol extract and sub-fractions: n-hexane, chloroform, ethyl acetate	*E. coli*, *S. aureus*, *S. typhi*, *S. flexneri*, *B. subtilis*, *A. niger*, *A. flavus*, *A. fumigatus*, *Fusarium solani*	DIZ_{MeOH} (1 mg/ml) 12–24 mm $DIZ_{Hex.}$ (1 mg/ml) 12–26 mm DIZ_{CHCl3} (1 mg/ml) 14–26 mm DIZ_{EtAC} (1 mg/ml) 21–26 mm	MIC_{MeOH} 2–3 mg/ml $MIC_{Hex.}$ 2.5–4 mg/ml MIC_{CHCl3} 2.5–3 mg/ml MIC_{EtAC} 2–3 mg/ml	Shah et al. (2015a, b)

T. africanum (leaves, flowers, stem) South Africa	Water, methanol, dichloromethane – methanol extracts (Maceration)	*B. cereus* ATCC 11778, *E. coli* ATCC 8739, *K. pneumoniae* ATCC 13883, *Moraxella catarrhalis* ATCC 23246, *P. aeruginosa* ATCC 27858, *S. aureus* ATCC 25923, *S. pyogenes* ATCC 8668	MIC 1– > 8 mg/ml (G^+ bacteria) MIC 0.125– > 8 mg/ml (G^- bacteria)	Not tested	Ruiters et al. (2016)
T. kraussii (leaves, flowers, stem) South Africa			MIC 0.8–6.6 mg/ml (G^+ bacteria) MIC 1–8 mg/ml (G^- bacteria)	Not tested	
T. trifidum (leaves, flowers, stem) South Africa			MIC 1– > 8 mg/ml (G^+ bacteria) MIC 1– > 8 mg/ml (G^- bacteria)	Not tested	
T. montbretii subsp. *pamphylicum* (aerial parts) Turkey	Methanol extract (Soxhlet)	*E. coli*, *S. typhi*, *Yersinia enterocolitica*, *S. aureus, S. pneumoniae*, *E. aerogenes, L. monocytogenes*, *Lactobacillus reuteri*, *L. acidophilus, Micrococcus luteus*	DIZ (10% extract) 13.5–22.5 mm	Not tested	Özkan et al. (2007)
T. flavum (flowers) Italy	Ethanol (80%) extract (Maceration)	32 clinical isolates and 8 standard strains of bacteria	MIC 1024–16,384μg/ml (G^+ bacteria) MIC 8192– > 16,384μg/ml (G^- bacteria)	Not tested	Acquaviva et al. (2018)
T. fruticans (flowers) Italy			MIC 256–8192μg/ml (G^+ bacteria) MIC 2048–8192μg/ml (G^- bacteria)	Not tested	
T. siculum (flowers) Italy			MIC 256–8192μg/ml (G^+ bacteria) MIC 1024–8192μg/ml (G^- bacteria)	Not tested	

(continued)

Table 12.2 (continued)

Teucrium species (part used)	Type of extract (extraction method)	Tested microorganisms	DIZ (tested concentration) range, MIC range		References
			Antibacterial activity	Antifungal activity	
T. oliverianum (aerial parts) Saudi Arabia	Methanol (80%) extract (Maceration)	*K. pneumoniae*, *P. vulgaris*, *P. aeruginosa*, *Serratia marcescens*, *B. cereus*, *M. luteus*, *M. roseus*, *S. aureus*, *A. flavus*, *A. ochraceus*, *C. albicans*, *F. moniliforme*	DIZ (10 mg/ml) 9 mm (*B. cereus*, *K. pneumoniae*)	Not active	Shahat et al. (2017)
T. orientale var. *glabrescens* Turkey	Water extract (Maceration)	*E. coli* ATCC 25922, *Y. pseudotuberculosis* ATCC 911, *P. aeruginosa* ATCC 43288, *S. aureus* ATCC 25923, *E. faecalis* ATCC 29212, *B. cereus* 709 Roma; *M. smegmatis* ATCC 607, *C. albicans* ATCC 60193, *S. cerevisiae*	DIZ 6–16 mm	Not active	Yildirmiş et al. (2017)
T. cubense (aerial parts) Mexico	Water extract (Maceration)	*S. aureus*, *S. haemolyticus*, *E. faecalis*, *P. aeruginosa*, *E. coli*, *Acinetobacter lwoffii*, *A. baumanii*, *Burkholderia cepacin*, *C. albicans*, *C. tropicalis*, *T. belgeii*	DIZ (375µg/disk) 22 mm (*A. lwoffii*) DIZ (750µg/disk) 10 mm (*P. aeruginosa*)	DIZ (750µg/disk) 12 mm (*C. albicans*)	Jacobo-Salcedo et al. (2011)
T. yemense (aerial parts) Yemen	Methanol, water extracts (Maceration)	*S. aureus* ATCC 6538, *B. subtilis* ATCC 6059, *M. flavus*, *E. coli* ATCC 11229, *P. aeruginosa* ATCC 27853, *C. maltose*, multiresistant strains – *S. epidermidis*, *S. haemolyticus*, *S. aureus*	DIZ_{MeOH} (4 mg/ml) 9–26 mm MIC_{MeOH} 250–500µg/ml DIZ_{H2O} (4 mg/ml) 10–16 mm MIC_{H2O} > 1000µg/ml	Not active	Mothana et al. (2009a, b)
T. sokotranum (aerial parts) (Soqotra Island) Yemen			DIZ_{MeOH} (4 mg/ml) 10–22 mm MIC_{MeOH} 500–1000µg/ml DIZ_{H2O} (4 mg/ml) 10–22 mm MIC_{H2O} 250–1000µg/ml	Not active	

T. persicum (aerial parts) Iran	Methanol extract (Maceration)	*E. coli* PTCC 1338, *B. subtilis* PTCC 1023, *S. aureus* PTCC 1112, *S. epidermis* PTCC 1114, *P. aeruginosa* PTCC 1074, *S. typhi* PTCC 1693, *K. pneumonia* PTCC 1031, *A. niger* PTCC 5010, C. *albicans* PTCC 5027	MIC 0.5–2 mg/ml	MIC 2 mg/ml	Javidnia et al. (2009)
T. leucocladum (aerial parts) Egypt	n-Hexane-ether extract (Maceration)	*E. coli*, *P. aeruginosa*, *S. aureus*, *B. subtilis*, *C. albicans*	DIZ (1 mg/ml) 16–19 mm	DIZ (1 mg/ml) 15 mm	El-Shazly and Hussein (2004)
T. botrys (aerial parts) Serbia	Methanol, acetone, ethyl acetate extracts (Maceration)	*S. aureus* ATCC 25923, *E. coli* ATCC 25922, *S. aureus*, *E. coli*, *P. aeruginosa*, *C. albicans* ATCC 10231, *C. albicans*, *A. niger*	MIC_{MeOH} 1.25 mg/ml (*S. aureus* ATCC) MIC_{AcOH} 2.5 mg/ml (*S. aureus* ATCC) MIC_{EtAC} > 10 mg/ml	MIC_{MeOH} > 20 mg/ml MIC_{AcOH} 10 mg/ml (*A. niger*) MIC_{EtAC} 5–10 mg/ml	Stanković et al. (2012)
T. bicolor (aerial parts) Mexico	Methanol extract (Maceration)	*C. albicans*, *C. parapsilosis*, *C. tropicalis*, *C. krusei*, *C. glabrata*, *M. tuberculosis*	MIC 125μg/ml (*M. tuberculosis*)	MIC 31.2–125μg/ml	Garza et al. (2017)
T. sauvagei (leaves) Tunisia	Methanol extract (Maceration)	Dermatophytes	Not tested	Active against dermatophytes	Salah et al. (2006)
T. royleanum (whole plant) Pakistan	Methanol extract and sub-fractions: n-butanol, chloroform, ethyl acetate (Maceration)	*E. coli*, *B. subtilis*, *K. pneumoniae*, *S. flexneri*, *S. aureus*, *S. typhi*, *P. aeruginosa*, *T. longifusus*, *C. albicans*, *C. glaberata*, *A. flavus*, *M. canis*, *F. solani*	DIZ_{MeOH} (3 mg/ml) 9–16 mm DIZ_{BuOH} (3 mg/ml) 5–6 mm DIZ_{CHCl3} (3 mg/ml) 4–24 mm DIZ_{EtAC} (3 mg/ml) 14–25 mm	MeOH (24 mg/ml) 40–50% of inhibition $CHCl_3$ (24 mg/ml) 53–87% EtAc (24 mg/ml) 40–71% BuOH (24 mg/ml) 70% (*T. longifusus*)	Ahmad et al. (2008)

Table 12.3 List of major oils' compounds, tested microorganisms, and results of *Teucrium* species essential oils antimicrobial activity

Teucrium species	Major oil's compounds	Tested microorganisms	DIZ (tested concentration) range, MIC range		References
			Antibacterial activity	Antifungal activity	
T. polium Iran	Limonene (37.70%), 2,4 di-tetra-butylphenol (10.81%) p-cymene (8.20%)	*Staphylococcus aureus*, *S. epidermidis*, *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, *Escherichia coli*	DIZ (10μl) 7–17 mm MIC 5–50μl	Not tested	Vahdani et al. (2011)
T. polium Algeria	Germacrene, bicyclogermacrene, *β*-pinene, carvacrol	*S. aureus* ATCC 25923, *Enterococcus feacalis* ATCC 29212, *Bacillus cereus* ATCC 11778, *E. coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *Aspergillus flavus*, *Fusarium oxysporum*, *Rhizopus stolonifer*	DIZ (15μl) 9–16 mm MIC 3–5μl/ml	2–10μl/ml – 6.58–25.9% of inhibition	Belmekki et al. (2013)
T. polium subsp. *capitatum* Italy (Corsica Island)	*α*-pinene (24.71%), *α*-thujene (8.1%), terpinen-4-ol (6.6%), limenone (5.2%)	*S. aureus*, *S. epidermidis*, *Listeria innocua*, *Campylobacter jejuni*, *Enterobacter aerogenes*, *E. aerogenes* (MDR)	DIZ (15μl) 10–44 mm MIC 0.2–12.5 mg/ml	Not tested	Djabou et al. (2013)
T. polium Iran	*β*-caryophyllene (29%), farnesene (13%), *β*-pinene (11%), germacrene D (6.5%), *α*-pinene (5.5%)	15 clinical isolates of *K. pneumoniae*	DIZ 14–28.5 mm MIC 0.62–1.25 mg/ml	Not tested	Raei et al. (2014)
T. polium Iran	*α*-pinene (25.79%), myrcene (12.50%)	*P. aeruginosa*, *Pantoea agglomerans*, *Brenneria nigrifluens*, *Rhizobium radiobacter*, *Rhizobium vitis*, *Streptomyces scabies*, *Ralstonia solanacearum*, *Xanthomonas campestris*, *Pectobacterium cartovorum*	Active against – *R. solanacearum*, *P. agglomerans*, *B. nigrifluens*, *S. scabies*	Not tested	Purnavab et al. (2015)

T. polium subsp. *capitatum* Algeria	t-cadinol (18.3%), germacrene D (15.3%), *β*-pinene (10.5%)	*S. aureus* ATCC 6538, *B. subtilis* ATCC 9372, *P. aeruginosa* ATCC 9027, *K. pneumoniae* ATCC 4352, *Candida albicans* ATCC 24433	DIZ (20μl) 14.7–35.3 mm	DIZ (20μl) 13.7 mm	Kerbouche et al. (2015)
T. polium Morocco	Not analysed	*S. aureus* ATCC 29213, *E. coli* ATCC 25922, *P. aeruginosa* ATCC 27853, *C. albicans* ATCC 10231, *A. brasiliensis* ATCC 16404	DIZ (10μl) 12 mm (*S. aureus*) MIC 1.3μl/ml (*S. aureus*)	DIZ (80μl) 10.33 mm (*C. albicans*)	Boukhira et al. (2016)
T. polium Turkey	(Z)-*β*-farnesene (15.49%), *β*-phellandrene (10.77%), *α*-farnesene (10.71%)	*S. aureus* (MRSA), *S. aureus* ATCC 6538, *P. aeruginosa*, *E. coli* O157:H7, *B. cereus*	DIZ (5μl) 11–15 mm	Not tested	Sevindik et al. (2016)
T. polium subsp. *gabesianum* Tunisia	*β*-pinene (35.9%), *α*-pinene (13.32%), *α*-thujene (8.46%)	*E. coli* ATCC 25922, *E. faecalis* ATCC 29212, *S. aureus* ATCC 25923, *P. aeruginosa* ATCC 27853, *Citrobacter freundeii*, *Proteus mirabilis C. albicans*, *Cryptococcus neoformans*, *Trichophyton rubrum*, *T. soudanense*, *Microsporum canis*, *A. fumigatus*, *Scopulariopsis brevicaulis*	MIC 0.078–0.156 mg/ml	MIC 0.062– > 1 mg/ml	Ben Othman et al. (2017)
T. marum subsp. *marum* Italy (Sardinia Island)	Isocaryophyllene (20.24%), *β*-bisabolene (14.73%), *β*-sesquiphellandrene (11.27%), *α*-santalene (10.97%), dolichodial (9.38%), *α*-caryophyllene (7.18%)	*F. oxysporum*, *Botrytis cinerea*, *Rhyzoctonia solani*, *Alternaria solani*	Not tested	MIC 250–3800μg/ml	Ricci et al. (2005)
T. marum Italy (Corsica Island)	Caryophyllene oxide (9.8%), (E)-*α*-bergamotene (8.2%), *β*-bisabolene (7.5%)	*S. aureus*, *S. epidermidis*, *L. innocua*, *C. jejuni*, *E. aerogenes*, *E. aerogenes* (MDR)	DIZ (15μl) 8–40 mm MIC 0.4–1 mg/ml	Not tested	Djabou et al. (2013)

(continued)

Table 12.3 (continued)

Teucrium species	Major oil's compounds	Tested microorganisms	DIZ (tested concentration) range, MIC range		References
			Antibacterial activity	Antifungal activity	
T. arduini Montenegro	Germacrene D (16.98%), *β*-caryophyllene (14.98%), *β*-burbonene (5.59%), *α*-amorphene (4.68%), linalool (7.05%), *α*-terpinolene (5.25%), 1-octene-3-ol (4.69%)	*B. subtilis*, *E. cloaceae*, *E. faecalis* ATCC 29212, *E. coli* ATCC 25922, *K. pneumoniae*, *M. lysodeikticus* ATCC 4698, *P. mirabilis*, *S. aureus* ATCC 25923, *S. aureus*, *C. albicans* ATCC 10259	MIC 6.25–50μl/ml	MIC 50μl/ml	Vuković et al. (2011)
T. arduini Croatia	*β*-caryophyllene (32.9%), germacrene D (16.4%), borneol (5.4%)	*S. aureus* ATCC 6538, *E. faecalis* ATCC 21212, *E. coli* ATCC 10535, *P. aeruginosa* ATCC 27853, *C. albicans* ATCC 10231, *M. gypseum, A. brasiliensis*	MIC 6.25–37.5 mg/ml	MIC 7.81–25 mg/ml	Kremer et al. (2012)
T. chamaedrys Italy (Corsica Island)	(E)-*α*-caryophyllene (33.9%), germacrene D (18.5%), *α*-humulene (7.5%), *δ*-cadinene (4.6%)	*S. aureus*, *S. epidermidis*, *L. innocua*, *C. jejuni*, *E. aerogenes*, *E. aerogenes* (MDR)	DIZ (15μl) 6–22 mm MIC 1– > 50 mg/ml	Not tested	Djabou et al. (2013)
T. chamaedrys subsp. *chamaedrys* Turkey	Germacrene D (16.7%), *α*-pinene (15.8%), *β*-caryophyllene (11.8%), *β*-pinene (8.9%), *β*-myrcene (4.1%)	*E. coli* ATCC 35218, *K. pneumoniae* ATCC 13883, *Yersinia pseudotuberculosis* ATCC 911, *Serratia marcescens* ATCC 13880, *E. faecalis* ATCC 29212, *S. aureus* ATCC 25923, *B. subtilis* ATCC 6633, *C. albicans* ATCC 60193, *C. tropicalis* ATCC 13803	DIZ (1000μg/ml) 5–15 mm	Not active	Küçük et al. (2006)
T. chamaedrys subsp. *lydium* Turkey	*β*-caryophyllene (19.7%), *α*-pinene (12.5%), germacrene D (9.3%), *β*-pinene (6.6%), caryophyllene oxide (6.1%)		DIZ (1000μg/ml) 5–15 mm	Not active	
T. orientale var. *puberulens* Turkey	*β*-caryophyllene (21.7%), 2-methyl cumarone (20.0%), germacrene D (10.6%), *α*-humulene (4.8%), *δ*-cadinene (4.1%)		DIZ (1000μg/ml) 5–15 mm	Not active	

T. orientale var. *orientale* Turkey	*β*-caryophyllene (15.3–19.0%), germacrene D (14.2–12.8%), caryophyllene oxide (14.0–19.0%)	*S. aureus* ATCC 29213, *E. faecalis* ATCC 29212, *E. coli* ATCC 25922, *P. aeruginosa* ATCC 27853, *C. albicans*, *C. tropicalis*	MIC 100–400μg/ml	MIC 25–50μg/ml	Kucukbay et al. (2011)
Teucrium orientale var. *puberulens* Turkey	*β*-caryophyllene (15.3–19.0%), germacrene D (14.2–12.8%), caryophyllene oxide (14.0–19.0%)		MIC 50–400μg/ml	MIC 12.5–25μg/ml	
T. massiliense Italy (Corsica Island)	6-methyl-3-heptyl acetate (19.1%), 3-octanyl acetate (7.0%), pulegone (6.9%), germacrene D (6.1%)	*S. aureus*, *S. epidermidis*, *L. innocua*, *C. jejuni*, *E. aerogenes*, *E. aerogenes* (MDR)	DIZ (15μl) 6–41 mm MIC 0.8–6 mg/ml	Not tested	Djabou et al. (2013)
T. scorodonia subsp. *scorodonia* Italy (Corsica Island)	(E)-*α*-caryophyllene (21.1%), germacrene B (8.3%), *α*-humulene (6.9%), germacrene D (6.7%), *α*-cubebene (6.2%)		DIZ (15μl) 6–26 mm MIC 0.2– > 50 mg/ml	Not tested	
T. flavum subsp. *glaucum* Italy (Corsica Island)	Limenone (27.4%), *α*-pinene (12.2%), (Z)-*α*-ocimene (6.0%), (E) phytol (4.5%)		DIZ (15 μl) 16–39 mm MIC 0.2–1.5 mg/ml	Not tested	
T. africanum South Africa	*β*-cubebene (20.5%), *α*-cubebene (29.3%)	*B. cereus* ATCC 11778, *E. coli* ATCC 8739, *K. pneumoniae* ATCC 13883, *Moraxella catarrhalis* ATCC 23246, *P. aeruginosa* ATCC 27858, *S. aureus* ATCC 25923, *S. pyogenes* ATCC 8668	MIC 0.16– > 8 mg/ml	Not tested	Ruiters et al. (2016)
T. kraussii South Africa	Not analysed		MIC 4 mg/ml (*S. pyogenes*)	Not tested	
T. trifidum South Africa	*β*-cubebene (31.1%), *α*-cubebene (11.4%), *β*-caryophyllene (7.7%)		MIC 2– > 8 mg/ml	Not tested	
T. leucocladum Egypt	Patchouli alcohol (31.24%), *β*-pinene (12.66%), *α*-pinene (10.99%), *α*-cadinol (19.27%), viridiflorol (5.36%), myrcene (5.35%)	*E. coli*, *P. aeruginosa*, *S. aureus*, *B. subtilis*, *C. albicans*	DIZ (20 mg/ml) 12–30 mm	DIZ (20 mg/ml) 26 mm	El-Shazly et al. (2004)

(continued)

Table 12.3 (continued)

Teucrium species	Major oil's compounds	Tested microorganisms	DIZ (tested concentration) range, MIC range		References
			Antibacterial activity	Antifungal activity	
T. stocksianum subsp. *stocksianum* Oman	α-cadinol (7.6%), β-selinene (6.4%), trans-verbenol (5.9%), caryophyllene oxide (5.7%), α-phellandren-8-ol (5.0%), verbenone (5.0%), δ-cadinene (5.1%)	*S. aureus* NCTC 6571, *E. coli* NCTC 10418, *P. aeruginosa* NCTC 10662, *S. aureus, S. albus*, *S. epidermidis*, *S. mitis*, *S. sanguis*, *M. luteus*, *B. subtilis*, *B. cereus*, *E. coli*, *E. aerogenes*, *K. pneumoniae*, *S. typhy*, *P. vulgaris*, *P. aeruginosa*, *C. albicans*, *Sacharomyces cerevisiae*, *R. stolonifer*, *Penicillium notatum*, *F. oxysporum*	DIZ (2 mg/disk) 9–18.5 mm MIC 4.5–5 mg/ml (G^+ bacteria) MIC 6.5–11 mg/ml (G^- bacteria)	DIZ (2 mg/disk) 3.5–6 mm	Hisham et al. (2006a, b)
T. mascatense Oman	Linalool (27.8%), linalyl acetate (12.6%), β-eudesmol (10.1%), α-bergamotene (5.0%)		DIZ (0.2 mg/disk) 3.5–17.5 mm MIC 1.5–2.5 mg/ml (G^+ bacteria) MIC 6–8.5 mg/ml (G^- bacteria)	DIZ (1.6 mg/disk) 3.5–6.5 mm	
T. hyrcanicum Iran	(E)-β-farnesene (34.1%)	*B. subtilis*, *S. aureus*, *S. typhi*, *P. aeruginosa*, *E. coli*, *A. niger*, *C. albicans*	Active against *B. subtilis*, *S. aureus*, *S. typhi*, *P. aeruginosa*	Active against *A. niger*	Morteza-Semnani et al. (2011)
T. ramosissimum Tunisia	β-eudesmol (44.52%), caryophyllene oxide (9.36%), α-thujene (5.51%), sabinene (4.71%), *t*-cadinol (3.9%)	*S. aureus* ATCC 25923, *E. faecalis* ATCC 29212, *E. coli* ATCC 25922, *S. enteridis* ATCC 13076, *S. typhymurium* NRRL B- 4420	MIC 0.24–0.36 mg/ml	Not tested	Ben Sghaier et al. (2007)
T. yemense Yemen	α-pinene (6.6%), (E)-caryophyllene (19.1%) α-humulene (6.4%), δ-cadinene (6.5%), caryophyllene oxide (4.3%), α-cadinol (9.5%), shyobunol (4.6%)	*E. coli* ATCC 10536, *P. aeruginosa* ATCC 25619, *S. aureus* ATCC 29737, *B. cereus*, *A. niger* ATCC 16888, *B. cinerea* ATCC 126943, *C. albicans* ATCC 90028	MIC 156–1250µg/ml	MIC 313–1250µg/ml	Ali et al. (2017)

T. sauvagei Tunisia	β-eudesmol, *t*-cadinol, α-thujene, gamma-cadinene, sabinene	Dermatophytes	Not tested	Active against dermatophytes	Salah et al. (2006)
T. divaricatum subsp. *villosum* Lebanon	(E)-caryophyllene (30.1%), caryophyllene oxide (6.1%)	G^+ bacteria, G^- bacteria	Active against G^+ bacteria	Not tested	Farmisano et al. (2010)
T. plectranthoides India	Not analysed	*B. megaterium*, *B. subtilis*, *E. coli*, *S. aureus, P. aeruginosa, P. vulgaris*, *A. niger, Xanthomonas campestris*, *A. parasiticus*, *Rhizopus oryzae*, *Rhizoctonia oryzae-sativae*, *Colletotrichum musae*, *F. solani*, *C. albicans*, *Alternaria brassicicola*	DIZ 20–38 mm	DIZ 16–27 mm	Thoppil et al. (2001)

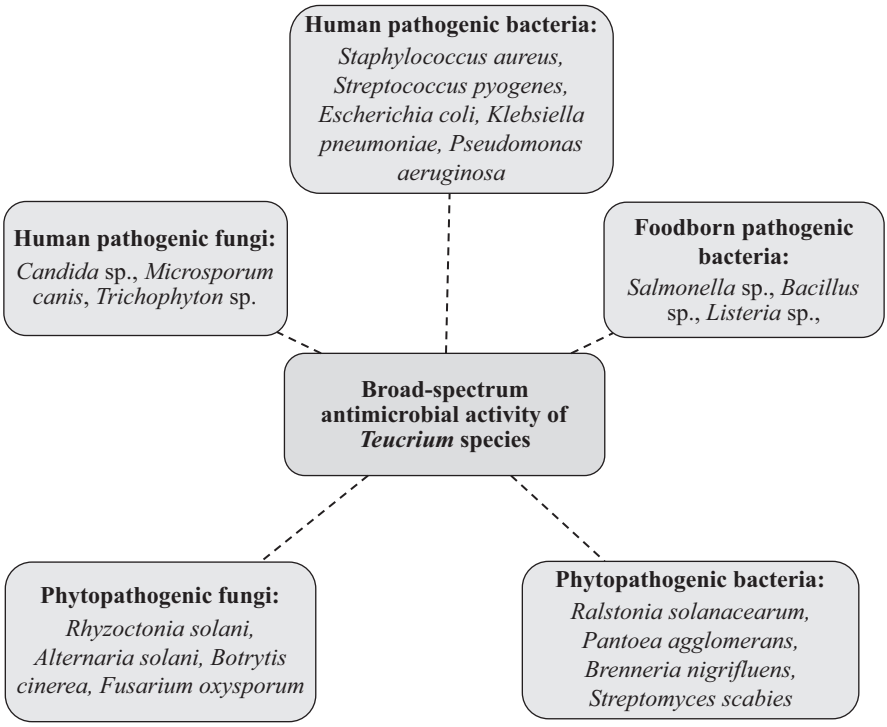

Fig. 12.4 The most susceptible bacteria and fungi to *Teucrium* species

necessary. So far, only, Elmasri et al. (2014, 2015) have evaluated antibiofilm activity of *Teucrium* species. The authors have noticed that several sesquiterpenes and flavonoids from *Teucrium polium* were effective in prevention of *Staphylococcus aureus* biofilm formation.

12.6.1 Antimicrobial Activity of Teucrium *Species Plant Extracts*

Generally, three levels of investigation of antimicrobial activity of plant extracts are established: (i) testing of crude extract, (ii) testing of sub-fractions, and (iii) testing of pure compounds. According to the literature search, crude extracts of *Teucrium* species were frequently researched. Several studies were focused on testing of sub-fractions of extracts, but no studies on testing of isolated pure compounds. Also, the mechanism of antimicrobial action of extracts from *Teucrium* species has not been determined yet.

The MIC values are used as cut-off points for classification of the antimicrobial potential of plant extracts. The one of that classification was defined by Tamokou

et al. (2017), as follows: MIC below 100μg/ml – highly active, 100 ≤ MIC ≤ 512μg/ml – significantly active, 512 < MIC ≤ 2048μg/ml – moderately active, MIC > 2048μg/ml – low active, MIC > 10 mg/ml – not active. The stated cut-off points were applied for interpretation of antimicrobial activity of extracts from *Teucrium* species. Summary results of antimicrobial activity are presented in Table 12.2. In the following paragraphs, the most significant results were discussed.

Teucrium polium was one of the most tested *Teucrium* species and plant materials, collected from different regions, have been screened for antimicrobial activity. Extracts from *Teucrium polium* originated from Tunisia and Turkey showed the most promising antimicrobial activity in relation to commonly used Gram-positive bacteria (*Staphylococcus aureus*, *S. epidermidis*, *Bacillus subtilis*, *B. cereus*, *Micrococcus luteus*, *Enterococcus faecalis*), Gram-negative bacteria (*Escherichia coli*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Salmonella typhi, Enterobacter cloaceae*) and fungi (*Candida albicans*, *Aspergillus niger*, *A. fumigatus*, *Trychophyton rubrum*). The MIC values of ethanol and water extract from Tunisian *Teucrium polium* were 0.156–0.625 mg/ml against bacteria and 0.625 mg/ml against fungal species *Microsporum canis* (Ben Othman et al. 2017). Moreover, Turkish *Teucrium polium* extract, in a form of decoction, showed better activity with MIC range of 16–64μg/ml for bacteria and 8–64μg/ml for fungi (Deliroman Orhan et al. 2012). The methanol extract from Jordanian plant showed moderate antibacterial activity, the best activity was noticed against *Escherichia coli* (MIC of 1.2 mg/ml) (Tarawneh et al. 2010). In addition, the ethanol extract of plant material from the same region were active on *Staphylococcus aureus* and *Pseudomonas aeruginosa* at MIC of 80 ppm (Khalil et al. 2009). On the other side, organic solvent extracts, tested in other studies, exhibited low antimicrobial activity or they were not active, MIC values were 3.125–50 mg/ml for bacteria and up to > 150 mg/ml for fungi (Hashem 2011; Stanković et al. 2012; Mirzei et al. 2013; Khaled-Khodja et al. 2014; Dridi et al. 2016). Using time-kill assay, the ethanol extract at concentration of 0.3 mg/ml has no effect on the growth of *Escherichia coli* O157 NCTC 1290 (Mashreghi and Niknia 2012). In the study of Mansouri (1999), *Teucrium polium* flower ethanol extract had very low antistaphylococcal activity. Against 489 isolates of *Staphylococcus aureus*, at concentration of 30 mg/ml, it showed activity against 0.61% of tested isolates. The antilisterial activity of ethanol extract was noticed, the inhibitory zones of 10–11 mm (at conc. 133 mg/ml) and MIC values 12.5–50μg/ml were detected (Altanlar et al. 2006). Against pathogenic bacteria, *Brucella melitensis*, the extracts of *Teucrium polium* showed moderate activity compared to other medicinal plants tested in the same study (Motamedi et al. 2010). Furthermore, the synergistic activity of *Teucrium polium* extract and antibiotics was investigated. The methanol extract in combination with antibiotics (amoxicillin, chloramphenicol, neomycin, doxycycline, clarithromycin, cephalexin, and nalidixic acid) enhanced the activity of antibiotics against the resistant *Escherichia coli* strain (Darwish and Aburjai 2010).

Studies on *Teucrium chamaedrys* extracts indicated their similar antimicrobial activity even that plant material was collected in the different regions of the world.

In general, low to moderate antimicrobial activity was noticed and activity was higher against Gram-positive bacteria then Gram-negative bacteria and fungi (Table 12.2). In the recent paper (Nastić et al. 2018), the authors have reported the activity of *Teucrium chamaedrys* extract obtained by supercritical water extraction. If we compare the results with the results of the study (Stanković et al. 2012) where plant material was extracted by maceration, the higher activity of supercritical water extract was obtained. The plant materials were from the same region (Serbia). In *Teucrium chamaedrys* supercritical water extract several phenolic compounds were identified: vanillin acid, caffeic acid, epicatechin, ferulic acid, sinapic acid, gallic acid, protocatechuic acid, catechin, and chlorogenic acid. In addition, in ethanol extract of *Teucrium chamaedrys* from Romania the following phenolic compounds, luteolin, p-coumaric acid, isoquercitrin, rutin, quercitrin, were isolated (Vlase et al. 2014).

Teucrium montanum is one of the most popular medicinal plants in Serbia. Two independent research groups investigated the antimicrobial activity of this plant and they observed that the extracts (methanol, acetone, ethyl acetate, butanol) were active against *Staphylococcus aureus* strains (MIC of 0.15–1 mg/ml) (Djilas et al. 2006; Stanković et al. 2012). In addition, the methanol, acetone, ethyl acetate extracts were not active against tested fungi (Stanković et al. 2012).

Teucrium arduini is an endemic Illyric Balkan species distributed in Croatia, Bosnia and Herzegovina, Montenegro, Serbia and northern Albania. Šamec et al. (2010) have conducted a detailed study including six different localities in Croatia. The leaf and flower infusions were tested. The lowest MIC values were found against *Staphylococcus aureus* ATCC 6538 (MIC of 1.56 and 4.16 mg/ml), depending on the location from which plant material (leaves) was collected. *Teucrium arduini* flower and leaf infusions did not exhibit activity against Gram-negative bacterial species, or against fungal species tested in this study. Except for water extract in form of infusion, antimicrobial activity of organic solvent extracts from different location (Croatia and Serbia) were tested and promising activity against Gram-positive bacteria (MIC of 0.15–2 mg/ml) was noticed (Stanković et al. 2012; Kremer et al. 2013). In Croatian samples of *Teucrium arduini* several phenolic compounds were identified: protocatechuic acid, 4-hydroxybenzoic acid, salicylic acid, gentisic acid, ferulic acid, vanillic acid, caffeic acid, syringic acid, sinapic acid, 4-coumaric acid, rosmarinic acid and quercetin (Kremer et al. 2013).

Two subspecies of *Teucrium scordium* (*T. scordium* subsp. *scordioides* and *T. scordium* subsp. *scordium*) have been subjected to antimicrobial testing of two research groups from Serbia. The plant material was collected from different localities and organic solvent extracts were prepared. The promising activity was noticed against *Staphylococcus aureus* ATCC 25922 (MIC of 0.3–0.6 mg/ml) (Kundaković et al. 2011; Stanković et al. 2012).

Numerous studies of antimicrobial activity of different *Teucrium* endemic species, rare species or species characteristic for a particular region were, also, performed. According to detected MIC values, extracts of *Teucrium flavum*, *T. fruticans*, *T. siculum*, *T. yemense*, *T. sokotranum* and *T. persicum* exhibited pronounced activity against tested Gram-positive bacteria, MIC range was 250–2000μg/ml

(Table 12.2). *Teucrium bicolor* methanol extract was active against *Mycobacterium tuberculosis* (MIC of 125μg/ml) and *Candida* species (MIC of 31.2–125μg/ml) (Garza et al. 2017). Three endemic species (*Teucrium africanum*, *T. kraussii* and *T. trifidum*) from southern Africa were active against some important pathogens; *Teucrium africanum* against *Escherichia coli* with MIC value of 0.13 mg/ml. *Teucrium kraussii* against *Streptococcus pyogenes* with MIC value of 0.8 mg/ml and *Teucrium trifidum* showed activity against *Pseudomonas aeruginosa* with MIC value of 0.5 mg/ml (Ruiters et al. 2016). Oppositely, extracts of *Teucrium oliverianum*, *T. orientale*, *T. royleanum* and *T. botrys* showed low activity (Table 12.2).

12.6.2 Antimicrobial Activity of Teucrium *Species Essential Oils*

Essential oils are recognized as the most active products of plant metabolism. They present the mixture of bioactive compounds including monoterpenes (hydrocarbons and oxygenated derivatives), sesquiterpenes (hydrocarbons and oxygenated derivatives) and aliphatic compounds (alkanes, alkenes, ketones, aldehydes, esters, and alcohols). Generally, essential oils have strong antimicrobial properties and could be used as food preservatives or therapeutic antimicrobial agents. The level of *Teucrium* essential oils bioactivity was determined according to cut-off points, it was estimated that MIC values lower than 2 mg/ml indicate significant activity of essential oils (Van Vuuren and Viljoen 2006). Hence, most of the essential oils from *Teucrium* species exhibited significant activity against Gram-positive bacteria (*Staphylococcus* sp., *Streptococcus* sp., *Bacillus* sp.) and Gram-negative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae, Salmonella* sp.) and fungi (*Candida* sp.). Essential oils were isolated from *Teucrium* plants originated from different regions, especially from the Mediterranean basin. It was obvious that the chemical composition and the amounts of main constituents (mono- and sesquiterpene hydrocarbons and oxygenated sesquiterpenes) differed notably and showing intraspecific variations in the chemical composition of the essential oils according to environment and/or genetic parameters. The essential oils' main compounds as well as detailed results of antimicrobial activity were summarized in Table 12.3. In the following sections, the most significant results were discussed.

Antibacterial activity of *Teucrium polium* essential oil was investigated in several studies. The oil in the quantity of 5–20μl inhibit the growth of *Staphylococcus aureus* and *Bacillus subtilis* (Vahdani et al. 2011; Belmekki et al. 2013; Djabou et al. 2013; Kerbouche et al. 2015; Boukhira et al. 2016; Sevindik et al. 2016). Moreover, *Teucrium polium* essential oil extracted from plant material collected in North Anatolia (Turkey) showed promising activity against *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus* (Sevindik et al. 2016). In addition, essential oil of *Teucrium polium* originated from Iran was active against clinical isolates of *Klebsiella pneumoniae* (Raei et al. 2014). Interestingly, *Teucrium*

polium and *T. marum* essential oils were active against some phytopathogenic bacteria and fungi (Ricci et al. 2005; Purnavab et al. 2015). Essential oil of *Teucrium marum* inhibits the growth of *Rhyzoctonia solani* at concentration of 250μg/ml. Furthermore, *Teucrium orientale*, *T. africanum*, *T. ramosissimum*, *T. mascatense* and *T. yemense* essential oils showed excellent activity against tested bacteria (Table 12.3). As promising antibacterial agents can be *Teucrium africanum* essential oil against *Streptococcus pyogenes* (MIC of 0.16 mg/ml), *Teucrium ramosissimum* against *Salmonella enterica, S. typhimurium, Escherichia coli* (MIC of 0.28–0.24 mg/ml), *Teucrium mascatense* and *T. yemense* against *Staphylococcus aureus* and *Bacillus subtilis* (MIC of 156μg/ml). Multi-drug resistant strain of *Enterobacter aerogenes* was susceptible to *Teucrium massiliense* and *T. scordonia* essential oil (MIC of 0.2–0.4 mg/ml) (Djabou et al. 2013). On the other side, *Teucrium stocksianum*, *T. kraussii*, *T. trifidum*, *T. leucoclada*, *T. chamedrys* and *T. arduini* exhibited low antibacterial activity (Table 12.3).

Antifungal activity of *Teucrium* essential oils was, especially, evaluated against *Candida* species and dermatophytes (Table 12.3). Essential oils of *Teucrium orientale* subsp. *orientale* and *T. orientale* subsp. *puberulens* could be promising anti-*Candida* agents. They were active at concentrations range of 12.5–50μg/ml (Kucukbay et al. 2011). In addition, *Teucrium polium* and *T. sauvagei* were active against tested dermatophytes (Salah et al. 2006; Ben Othman et al. 2017).

Essential oils obtained from *Teucrium* species possess significant broad-spectrum antimicrobial activity, however, there is limited information available about their mechanisms of action. Better understanding the mechanisms of action will give more detailed information about their potency and potential application as antimicrobial agents.

12.7 Conclusion

This chapter provides a detailed review of the antimicrobial activity of *Teucrium* species, their active constituents, and their potential as sources of antibacterial and antifungal agents. The relevant literature summary showed that *Teucrium* species exhibited a diverse range of antimicrobial properties. The promising activity and potential application in control of bacteria and fungi possess the following species: plant extracts of *Teucrium polium*, *T. flavum*, *T. fruticans*, *T. siculum*, *T. yemense*, *T. sokotranum*, *T. persicum*, *T. scordium*, and essential oils from *Teucrium polium, T. orientale*, *T. africanum*, *T. ramosissimum*, *T. mascatence*, *T. yemense*, *T. massiliense*, *T. scordonia*. They were active against important pathogenic bacteria (*Staphylococcus* sp., *Bacillus* sp., *Enterococcus* sp., *Streptococcus* sp., *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Salmonella* sp.) and fungi (*Candida* sp., *Trychophyton* sp.). However, these results are conducted on the basis of in vitro studies. The future studies on mechanisms of action of plant extracts, essential oils, and pure active compounds will contribute to the development of new *Teucrium* antimicrobial agents. Furthermore, in vivo testing of activity, toxicity and

bioavailability will determine their actual relevance for treatment of infectious diseases or used as food preservatives.

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