Plant disease outbreaks cause global economic losses by reducing the quality and quantity of marketable plants and plant products. Plant diseases cause loss of crops, which leads to hunger and starvation of impoverished people, especially in less developed countries where there is limited access to disease control methods. In these countries, major crops usually suffer annual losses of about 30%–50% (Dubey et al., 2011). Although plant pathogenic bacteria are less harmful than fungi or viruses, they do cause many serious diseases in plants throughout the world (Anderson et al., 2004; Vidaver and Lambrecht, 2004).

*Ralstonia solanacearum* species complex (RSSC), formerly known as *Pseudomonas solanacearum* (Smith 1896) Smith (1914) or *Burkholderia solanacearum* (Smith 1896) (Safni et al., 2014) in the 20th century, was first described by Erwin F. Smith in 1896 as the causative agent of bacterial wilt in solanaceous plants (Genin, 2010; Mohumad Tahat and Sijam, 2010). It is one of the most important soil-borne plant pathogenic bacteria, and its appearance makes it the second most important bacterial pathogen on scientific and economic grounds (Mansfield et al., 2012). RSSC causes bacterial wilt on tomato and many other crops in tropical and subtropical regions, leading to huge economic losses. The bacterium, RSSC, has a large host range...
of more than 50 botanical families that represent more than 200 plant species, including tomato, potato, eggplant, pepper, peanut, tobacco, banana, groundnut, olive, and ginger (Genin, 2010; Ramsubhag et al., 2012; Vu et al., 2013).

RSSC is the cause of bacterial wilt disease that destroys many crops, leading to serious economic losses. Direct yield losses differ significantly according to the host, cultivar, climate, soil type, cropping pattern, and strain. Yield losses vary from 0%–91% for tomato, 33%–90% in potato, 10%–30% in tobacco, 80%–100% in banana, and up to 20% in groundnut (Elphinstone, 2005; Yuliar et al., 2015). Tomato crops have high economic value; therefore, it is essential to control bacterial wilt of tomato.

It is difficult to control bacterial wilt because of the complex nature of the pathogen. It can grow endophytically and survive in soil, and it has a wide host range and biodiversity (Singh et al., 2015; Yuliar et al., 2015). To control bacterial wilt disease, different methods have been prescribed till date (Yuliar et al., 2015). Yuliar et al. (2015) reported that studies conducted between 1984 and 2014 described the following methods to control bacterial wilt: biological methods (54%) were most commonly used, followed by cultural practices (21%), chemical methods (8%), and physical methods (6%).

Most researchers are interested in developing biological methods that involve the use of biological control agents (BCAs) and organic matter. Modes of action of BCAs are characterized by various interactions, such as the competition for nutrients and space, antibiosis, parasitism, and induced systemic resistance (Yuliar et al., 2015). Previous studies reported that beneficial microbes, such as species of *Pseudomonas*, *Bacteriophages*, *Streptomyces*, *Acinetobacter*, *Enterobacter*, *Bacillus*, and *Paenibacillus*, suppressed the growth of RSSC in field conditions. Therefore, the interest of researchers in BCAs has increased steadily (Chen et al., 2013; Yuliar et al., 2015). However, the biocontrol efficiencies of some BCAs are too low to be commercially available. This might be due to the poor colonization ability of antagonistic strains under different field conditions. The performance of BCAs is hindered by some difficulties, which are associated with the production, storage, and subsequent application of BCAs (Singh et al., 2015; Yuliar et al., 2015). Many previous studies reported that bacterial wilt was suppressed by organic matter. To suppress bacterial wilt, plant residues (80%) such as fresh plant materials, plant extracts, isolated compounds, and essential oils, have been most commonly used, followed by animal wastes (10%), and simple organic compounds (10%) (Yuliar et al., 2015).

Plant kingdom is the most efficient producer of different biologically active compounds (Dubey et al., 2011). Plants contain abundant bioactive materials, such as secondary metabolites, volatile oils, and essential oils. Since plants are an important source of bioactive materials, they can be exploited to develop new biopesticides (Bhagat et al., 2014; Gurjar et al., 2012). In the development of novel pesticides, secondary metabolites could be used as lead compounds as they have novel modes of action (Bourgaud et al., 2001; Dubey et al., 2011). The extracts obtained from various plant species have promising potential applications: they can be used as natural products to fight plant pathogens in agriculture (Bhagat et al., 2014; Gurjar et al., 2012; Pretorius and van der Watt, 2011). However, very few natural plant products have been developed from screening programs on a commercial scale (Pretorius and van der Watt, 2011). Only a handful of pesticidal plant products have been successfully used on a commercial scale; they constitute a very small percentage (<0.1%) of total pesticide products (Glare et al., 2012; Isman, 2006; Sola et al., 2014). Pyrethrum, rotenone, neem, and essential oils are the four major types of botanical pesticide products currently used to control plant diseases. Furthermore, ryania, nicotine, and sabadilla are the other three botanical pesticides used to a limited extent in different countries along with plant extracts and oils, such as garlic oil (El-Wakeil, 2013; Tanwar et al., 2012).

In most research studies, scientists have performed *in vitro* assays in potted plants to determine the efficacy of various botanicals (extracts and isolated compounds) in controlling RSSC. However, only a handful of antibacterial substances were examined to determine whether they can control bacterial wilt disease in tomato. Most of studies have been focused on isolation and determination of antibacterial substances from plants to control bacterial wilt diseases. These plant-derived products are listed in Table 1 and Table 2, and chemical structures in Fig. 1. Several previous studies have reported that some plant materials, which were incorporated as organic amendments in soil, suppressed the growth of RSSC, such as *Brassica* sp. (cole) (Olivier et al., 2006), *Azadirachta indica* (neem) (Pontes et al., 2012).
Table 1. Plant extracts showing a potent in vitro antibacterial activity against *Ralstonia solanacearum* species complex (RSSC) causing bacterial wilt

<table>
<thead>
<tr>
<th>Plant species</th>
<th>Part used</th>
<th>Plant extract*</th>
<th>Strain (host)</th>
<th>Method</th>
<th>Antibacterial activity†</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Azadirachta indica</em> (neem)</td>
<td>Leaf</td>
<td>MeOH</td>
<td>RSSC (tomato)</td>
<td>Agar well diffusion</td>
<td>DIZ: 18.4–21.6 mm</td>
<td>Murthy et al., 2015b</td>
</tr>
<tr>
<td><em>Allium sativum</em> (garlic)</td>
<td>Leaf, bulb</td>
<td>Aq.</td>
<td>RSSC (tomato)</td>
<td>Agar well diffusion</td>
<td>DIZ: 49 mm</td>
<td>Gopalakrishnan et al., 2014</td>
</tr>
<tr>
<td><em>Carica papaya</em> (papaya)</td>
<td>Seed</td>
<td>Aq, MeOH</td>
<td>RSSC (n.d.)‡</td>
<td>Agar well diffusion</td>
<td>DIZ: 19 mm</td>
<td>Uma et al., 2012</td>
</tr>
<tr>
<td><em>Eugenia jambolana</em> (Jamun)</td>
<td>Rhizome</td>
<td>Aq.</td>
<td>RSSC (tomato)</td>
<td>Agar well diffusion</td>
<td>DIZ: 20–26 mm MIC: 2–20 µg/ml</td>
<td>Murthy et al., 2015a</td>
</tr>
<tr>
<td><em>Curcuma longa</em> (turmeric)</td>
<td>Rhizome</td>
<td>Aq.</td>
<td>RSSC (tomato)</td>
<td>Agar well diffusion</td>
<td>Broth microdilution</td>
<td></td>
</tr>
<tr>
<td><em>Rhus chinensis</em> (Chinese sumac)</td>
<td>Gallnut</td>
<td>Aq.</td>
<td>RSSC EPS-1 (eggplant)</td>
<td>Agar dilution</td>
<td>MIC: 50 µg/ml</td>
<td>Feng et al., 2012</td>
</tr>
<tr>
<td><em>Acacia auriculiformis</em></td>
<td>Leaf</td>
<td>EtOH, Ac.</td>
<td>RSSC Rs-08-17 (eggplant)</td>
<td>Agar well diffusion</td>
<td>DIZ: 23.6–25.0 mm</td>
<td>Gaitonde and Ramesh, 2016</td>
</tr>
<tr>
<td><em>Anacardium occidentalis</em></td>
<td>Leaf</td>
<td>EtOH, MeOH</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Boerhavia diffusa</em></td>
<td>Whole plant</td>
<td>EA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Calotropis gigantea</em></td>
<td>Leaf</td>
<td>EtOH</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Cinnamomum zevlancium</em></td>
<td>Leaf</td>
<td>EtOH, EA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Cymbopogon flexuosus</em></td>
<td>Leaf</td>
<td>EA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Garcinia indica</em></td>
<td>Leaf</td>
<td>EtOH, MeOH, Ac.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Lawsonia inermis</em></td>
<td>Leaf</td>
<td>MeOH</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Mimosa pudica</em></td>
<td>Leaf</td>
<td>EtOH</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Psidium guajava</em></td>
<td>Leaf</td>
<td>EtOH, MeOH, Ac.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Tamarindus indica</em></td>
<td>Leaf</td>
<td>EtOH, MeOH, Ac.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*MeOH, methanol; Aq., aqueous; EtOH, ethanol; Ac., acetone; EA, ethyl acetate.
†DIZ, diameter of inhibition zone; MIC, minimum inhibitory concentration.
‡n.d., not determined.
**Table 2.** Plant metabolites showing a potent *in vitro* antibacterial activity against *Ralstonia solanacearum* species complex (RSSC) causing bacterial wilt

<table>
<thead>
<tr>
<th>Plant species</th>
<th>Part used</th>
<th>Plant metabolite*</th>
<th>Strain (host)</th>
<th>Method</th>
<th>Antibacterial activity†</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Macleaya cordata</em></td>
<td>Leaf</td>
<td>Essential oil</td>
<td>RSSC GMI 1000 (tomato)</td>
<td>Broth microdilution</td>
<td>MIC: 125 µg/ml</td>
<td>Li and Yu, 2015</td>
</tr>
<tr>
<td><em>Syzygium aromaticum</em></td>
<td>n.d.†</td>
<td>Essential oil</td>
<td>RSSC (tomato)</td>
<td>Agar well diffusion</td>
<td>DIZ: 52 mm</td>
<td>Gopalakrishnan et al., 2014</td>
</tr>
<tr>
<td><em>Clausena lansium</em></td>
<td>Seed</td>
<td>Lansiumamide B</td>
<td>RSSC (tobacco)</td>
<td>Agar dilution</td>
<td>MIC: 125 µg/ml</td>
<td>Li et al., 2014</td>
</tr>
<tr>
<td><em>Cryptomeria japonica</em></td>
<td>Wood</td>
<td>Ferruginol</td>
<td>RSSC no. 8224 (n.d.)</td>
<td>Agar dilution</td>
<td>MIC: 32 µg/ml, MIC: 8 µg/ml</td>
<td>Matsushita et al, 2006</td>
</tr>
<tr>
<td><em>Dalbergia odorifera</em></td>
<td>Wood</td>
<td>Liquiritigenin</td>
<td>RSSC (n.d.)</td>
<td>Agar disc diffusion</td>
<td>DIZ: 12.2 mm, DIZ: 14.2 mm, DIZ: 16.6 mm</td>
<td>Zhao et al., 2011</td>
</tr>
<tr>
<td><em>Salvia miltiorrhiza</em></td>
<td>Root</td>
<td>Protocatechuic acid</td>
<td>RSSC (tobacco)</td>
<td>Agar dilution</td>
<td>MIC: 20 µg/ml, MBC: 40 µg/ml</td>
<td>Li et al., 2016</td>
</tr>
<tr>
<td><em>Sedum takesimense</em></td>
<td>Arial part</td>
<td>Gallic acid</td>
<td>RSSC (tomato)</td>
<td>Broth microdilution</td>
<td>MIC: 50 µg/ml, MIC: 30 µg/ml, MIC: 100 µg/ml, MIC: 80 µg/ml</td>
<td>Vu et al., 2013</td>
</tr>
<tr>
<td><em>Syringa oblata</em></td>
<td>Flower bud</td>
<td>Eugenol</td>
<td>RSSC (tobacco)</td>
<td>Oxford cup</td>
<td>DIZ: 18.5 mm</td>
<td>Bai et al., 2016</td>
</tr>
<tr>
<td><em>Warbugia ugandensis</em></td>
<td>Stem bark</td>
<td>Mukaadial</td>
<td>RSSC (sweet potato)</td>
<td>Agar disc diffusion</td>
<td>MIC: 25 µg/ml, MIC: 25 µg/ml, MIC: 100 µg/ml, MIC: 100 µg/ml</td>
<td>Opiyo et al, 2011</td>
</tr>
</tbody>
</table>

*Plant metabolite includes essential oil and isolated compound.
†MIC, minimum inhibitory concentration; DIZ, diameter of inhibition zone; MBC, minimum bactericidal concentration.
†n.d., not determined.
Fig. 1. Chemical structures of isolated compounds showing a potent \textit{in vitro} antibacterial activity against \textit{Ralstonia solanacearum} species complex causing bacterial wilt.
2011), *Cajanus cajan* (pigeon pea), and *Crotalaria juncea* (sunn hemp) (Cardoso et al., 2006). The possible mechanism of action of plant residues primarily includes antimicrobial activities. Thereafter, the plant residues suppress pathogens indirectly by improving the physical, chemical, and biological soil properties (Cardoso et al., 2006). Presently, only a few isolated compounds have been used to control tomato bacterial wilt *in planta* or in field conditions (Li et al., 2016).

To the best of our knowledge, there are no effective chemical treatments and commercially available botanical products to control tomato bacterial wilt. In this study, we review plant-derived bactericides, including plant extracts (or residues), essential oils, and secondary metabolites, showing a potent *in vivo* antibacterial activities (in potted plants or in field) against tomato bacterial wilt caused by RSSC. Please note that these plant-derived bactericides have not yet been commercialized.

**Plant Extracts**

**Allium fistulosum.** *Allium* genus plants have antimicrobial properties, so they have been used in traditional medicine. Disease control efficacy of the aqueous extracts of *A. fistulosum* was evaluated against tomato bacterial wilt in a growth chamber. The soil pretreated with *A. fistulosum* extracts significantly reduced RSSC populations. The extracts also significantly reduced the incidence of tomato bacterial wilt (Deberdt et al., 2012).

**Chamaecyparis obtusa** (hinoki). *Chamaecyparis obtusa* (hinoki) is a perennial tree widely grown in the forests of Asian countries. The bark of this plant hardly decomposes. The bark has a fibrous structure and suggested rephrase an acidic pH (5.6), so it is used as a substrate in soilless culture, which decreases the losses caused by root-infecting pathogens (Terada, 1993). Ethanol extracts of the hinoki bark exhibited significant *in vitro* antibacterial activity against RSSC. The proliferation of RSSC was mainly inhibited by volatile oils and non-volatile substances of the bark. However, the activity of non-volatile substances was greater in inhibiting RSSC. In addition, the incidence of tomato bacterial wilt was greatly reduced by hinoki bark (Yu and Komada, 1999). Yu and Komada (1999) also found that hinoki bark could greatly reduce the crown and root rot of tomato, which is caused by the fungus *Fusarium oxysporum* f. sp. *radicis-lycopersici.*

**Eichhornia crassipes and other invasive alien species (IAS) in Ethiopia.** Invasive alien species (IAS) such as *Eichhornia crassipes* are a major problem in Ethiopia. They have a negative impact on the environment, especially hampering the country’s biodiversity. Alemu et al. (2013) reported that *E. crassipes* showed the highest antibacterial activity against RSSC as compared to other IAS, including *Mimosa diplotricha, Lantana camara,* and *Prosopis juliflora.* In the *in vivo* experiment, the three extracts applied at the time of inoculation showed the best antibacterial activity against tomato bacterial wilt with a control value of 91% for *E. crassipes,* and 71%–85% for the other plant extracts.

**Sedum takesimense.** The methanol extract of *S. takesimense* showed potent *in vitro* antibacterial activity against RSSC (Vu et al., 2013). Eight antibacterial gallotannins were isolated from the plant extract and identified as follows: gallic acid (1), methyl gallate (2), 4,6-di-O-galloylarbutin (3), 2,6-di-O-galloylarbutin (4), 2,4,6-tri-O-galloylglucose (5), 1,3,4,6-tetra-O-galloyl-β-glucose (6), 1,2,4,6-tetra-O-galloyl-β-glucose (7), and 1,2,3,6-tetra-O-galloyl-β-glucose (8). The minimum inhibitory concentration (MIC) values of these eight chemicals against RSSC varied between 0.02 to 0.10 g/l. Compound 8 showed maximum antibacterial activity against the plant pathogen. The antibacterial activity of galloylarbutins and galloylglucoses was enhanced by increasing the number of galloyl groups and substituents at 1 or 2 position of the glucose ring, respectively. Furthermore, the several combinations of compounds showed synergistic or partial synergistic effects.

On the other hand, the wettable powder formulation of the ethyl acetate layer of *S. takesimense* (ST-WP) effectively suppressed the development of tomato bacterial wilt in greenhouse experiment (Vu et al., 2013). Seven and 14 days after inoculation, the control efficacy of the formulation was 93.9% and 53.9% at 400-fold dilution, respectively. Its disease control efficacy was higher than that of agricultural streptomycin sulfate (200 µg/ml).
Plant Metabolites

Thymol, palmarosa oil, and lemongrass oil. Pradhanang et al. (2003) reported that thymol (a major component of thyme oil that is produced synthetically), palmarosa, and lemongrass oils were effective in reducing RSSC populations in infested soil, thereby minimizing the incidence of tomato bacterial wilt. The growth of RSSC in infested soils was completely inhibited seven days after the soil was treated with these essential oils and thymol component at a concentration of 0.4 ml (or g) per liter. Plants grown in this oil-treated soil did not wilt throughout the experiment (28 days after inoculation). Furthermore, plants grown in soil treated with 700 µg/ml of thymol were free from wilt and RSSC. Ten percent of plants grown in soil treated with palmarosa or lemongrass oil harbored the bacteria but did not wilt (Pradhanang et al., 2003).

Ji et al. (2005) also reported that the incidence of bacterial wilt was significantly reduced by application of 0.7% thymol on the susceptible cultivar Solar Set. They suggested that thymol can be used as a soil biofumigant for the management of RSSC.

Clove oil. Clove oil is an essential oil that is extracted from the buds of *Eugenia caryophyllata* (or formerly *Syzygium aromaticum*). It is widely used in traditional medicine and in the fragrance and flavoring industries. The major components of clove oil include eugenol, β-caryophyllene, and eugenyl acetate. It also contains lesser amounts of other components. Previous studies have reported that clove oil and its components possess many biological activities, including antibacterial, antifungal, antiviral, antioxidant, anaesthetic, and insecticidal activities (Chaieb et al., 2007).

Lee et al. (2012) proved that clove oil exhibited potent *in vitro* antibacterial activities against RSSC. The disease suppression efficacy of the essential oil was evaluated *in planta* using detached tomato leaves. The incidence of tomato bacterial wilt was significantly decreased using 0.005%–0.01% clove oil (Lee et al., 2012).

Cinnamon oil. Cinnamon belongs to *Cinnamomum* genus of the Lauraceae family. Most members of this family are used as spices. Cinnamon has been used as a spice in food preparations and in traditional medicine since ancient times. It has strong antioxidant, antibacterial, antifungal, antipyretic, anticancer, and anti-inflammatory properties. Cinnamon essential oil is extracted from the bark of cinnamon trees. Cinnamaldehyde (about 64%–90%) is the major component of cinnamon essential oil (Hamidpour et al., 2015).

In the series of experiments performed by Lee et al. (2012), cinnamon oil exhibited the highest *in vitro* antibacterial activity against RSSC, compared with other essential oils. *In planta*, cinnamon oil (0.01%) also significantly decreased the development of bacterial wilt disease three days after inoculation, and the disease protection effect still existed five days after inoculation. However, cinnamon oil (0.02%) caused phytotoxic effect on tomato petioles (Lee et al., 2012).

Methyl gallate. Methyl gallate was isolated from the methanol extract of *Toxicodendron sylvestre*. It significantly inhibited RSSC *in vitro* and *in planta* (Yuan et al., 2012). It exhibited antibacterial activity against RSSC, with MIC and minimum bacteriocidal concentration values of 20 and 30 µg/ml, respectively. In greenhouse experiments, its control efficacy, at 500 µg/ml, was 65.2%, which was significantly higher than that of agricultural streptomycin sulfate.

In other study, methyl gallate was isolated from the aqueous extract of *Rhus chinensis* (Chinese sumac or gallnut). Using agar dilution method, it was found that methyl gallet exhibits potent *in vitro* antibacterial activities against RSSC and other plant pathogens, including *Acidovorax citrulli*, *Xanthomonas citri pv. citri*, and *X. euvesicatoria* (MIC=50–100 µg/ml) (Feng et al., 2012). The mechanism of action of methyl gallate against RSSC was found to be as follows: the structure of cell walls in RSSC was damaged by methyl gallate; it also inhibited protein synthesis and succinate dehydrogenase activity in the pathogen (Fan et al., 2014).

Conclusions

The demand for environmentally acceptable, safe and effective pesticides is increasing in agriculture because of numerous problems associated with danger of human health and environment, poisonous effects by pesticide residues on food, and antibiotic resistance caused by using chemical pesticides. As one of biocontrol methods for the control of bacterial wilt
caused by RSSC, botanical bacteriocides can be promising tools. Most recent studies that revealed plant-derived products and metabolites showing potent antibacterial activity against RSSC were conducted in in vitro tests or in potted plants, but not in fields. Additionally, several problems such as the limitation of information available on application, efficacy and safety of most of botanical products, and the narrow range of formulation types and antimicrobial spectra should still be overcome for the development of commercial products using botanicals (Sola et al., 2014). Therefore, future areas of interest consist of field trials to assess the practical applicability of the botanical pesticides, development of optimized formulations with enhanced activity, and biosafety studies to ascertain their toxicity to humans, animals and crop plants. On the other hands, plant secondary metabolites can play an important role as lead molecules for chemical synthesis. This requires the continuous studies on the discovery of novel bacteriocidal compounds.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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