Plant Disease Management by Bioactive Natural Products

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Abstract

The expansion in population and economies leads to development of new methods of agriculture to increase the productivity and meet the demand. Chemical fertilizers and pesticides are used in large scale to increase the production, but these pose environmental impacts on different ecosystems of life. Bioactive natural products derived from microorganisms and plants serve to minimize these impact. Various compounds isolated from plant sources, algal sources, microbial sources, marine sources, etc., act as elicitors for plant defense against various sources. Majority of them are chitosan, salicylic acid (SA), benzoic acid, benzothiadiazole, alkaloids, flavonoids, terpenes, proteins, peptides, blasticidin, mildiomycin, polyoxins, phenolic compounds, etc., which act against various plant diseases caused by bacteria, fungi, and viruses. The present chapter discusses the usages of bioactive natural products as tool agonists pant disease management. These derived bioactive compounds minimize the use of chemical agents and contribute to eco-friendly sustainable agriculture practices.

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2.1 Introduction

Exponential rise in global population contributes to new aspects of food production to overcome the growing needs (Mancosu et al. 2015; McKenzie and Williams 2015). Worldwide, out of seven persons, one is chronically undernourished. Therefore, overcoming food challenge stands as a major issue globally (McCarthy et al. 2018; D'Odorico et al. 2018). There are various challenges including weed and pest management and other phytopathogens which form an important basis for regulation of crop production and development (Damalas and Eleftherohorinos 2011; Grasswitz 2019). As population and economies expand, new methods of agriculture are developed and implemented to increase the productivity (Thornton 2010). Chemical fertilizers and pesticides are used in large scale to increase the production, but these pose various environmental impacts on different ecosystems of life (Aktar et al. 2009; Zhang et al. 2018). Most of the developed countries are strict in or ban the use of toxic chemical fertilizers and pesticides and have initiated various programs on integrated pest management (Rijal et al. 2018). Along with this, their focus remains on the development of natural product–based pesticides from the plant extracts and essential oils (George et al. 2014; Walia et al. 2017). Development of bioactive natural products for the development of pesticides is an eco-friendly and cost-effective process with no metabolite formation after action (Atanasov et al. 2015; Chaudhary et al. 2017). In modern agriculture, bioactive natural products derived from microorganisms and plants serve to minimize the impact of phytopathogens (Strobel and Daisy 2003). It is recommended to use the bioactive natural products in combination with other products for effective control and to minimize the tolerance by the pathogens (Hintz et al. 2015). The US Environmental Protection Agency defines biopesticides as compounds derived from natural compounds and categorized biopesticides as either microbial biopesticides or biochemical biopesticides (Chandler et al. 2011; Marrone 2019). Biopesticides are nontoxic to nontarget pests and have minimal toxicity to the environment and humans (Quarcoo et al. 2014). The phytochemicals derived from natural products cover wide range of various chemical groups such as peptides, proteins, saponins, vitamins, terpenes, polysaccharide, and polyphenols which act as natural inducers in host defense systems (Mujeeb et al. 2014; Shad et al. 2014).

Bioactive natural products play an important role in disease prevention and healthcare systems (Sofowora et al. 2013). The characterization of bioactive compounds and natural products has utilized various chemical methods and spectroscopic techniques to determine their structures (Altemimi et al. 2017; Tyśkiewicz et al. 2019). The use of infrared spectroscopy and ultraviolet spectrophotometry, mass spectroscopy, nuclear magnetic resonance, high-performance liquid chromatography, circular dichroism, and polarimetry provides additional information about

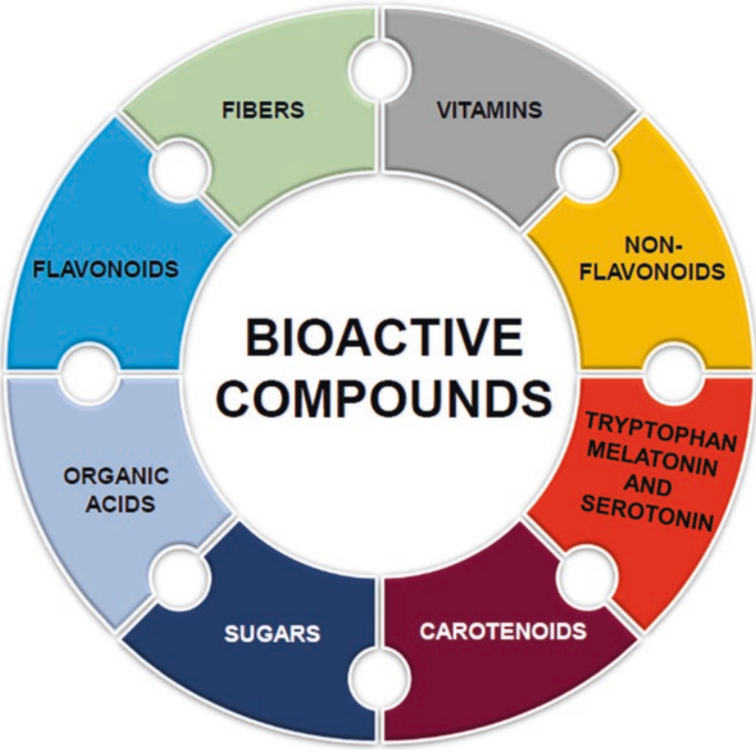

Fig. 2.1 Various bioactive molecules isolated from different natural sources

the various functional groups present in the bioactive compounds (Dias et al. 2016; Abu Khalaf et al. 2019). This chapter is designed to cover various bioactive natural products, their sources and types, and their mode of action. Efforts have also been made to summarize the role of bioactive natural compounds in plant defense mechanism in both indirect and direct methods. Various bioactive molecules isolated from different natural sources are well represented in Fig. 2.1.

2.2 Types of Bioactive Natural Products

Most of the bioactive natural products originate from microbes, animals, or plants, or they have prebiotic origin (Davies 2013; Davani-Davari et al. 2019). Microorganism and plants have proven to be good source of natural products such as bioinsecticides, antimicrobial agents, and antineoplastic agents (Cowan 1999; Hintz et al. 2015). Bioactive natural products derived from these sources are also reported to have various biological activities related to human health including biofilm inhibitory, anti-inflammatory, immunosuppressive, anticancer, antifungal, and antibiotic activities (Xu 2015; Pham et al. 2019). These products also possess selectivity,

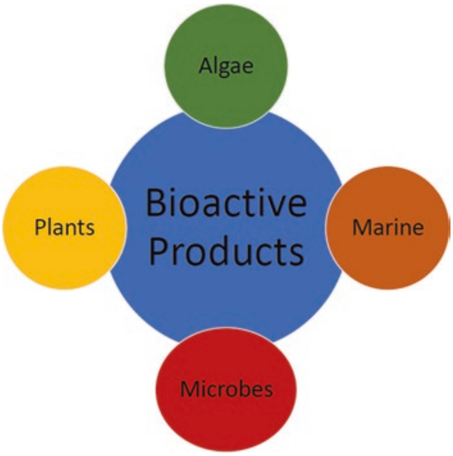

Fig. 2.2 Different sources of bioactive natural products for plant diseases

pharmacokinetic, and biopotency traits which act as drug traits (Guo 2017). Depending upon their type of source, they are categorized into microbial-, plant-, algal-, and marine-derived natural products (Fig. 2.2) (El Gamal 2010; Malve 2016).

2.2.1 Microbial-Derived Natural Products

Discovery of penicillin in 1929 opened the gates for microbial populations as a potent drug candidate (Tan and Tatsumura 2015). Till now, various microbial species have been screened and isolated for drug discovery which serves as antibacterial, antidiabetic, and anticancer agents, etc. (Raja et al. 2010; Cragg and Newman 2013). Genus *Streptomycetes* of the family Actinobacteria has been reported for the majority of naturally producing antibiotic agents (Barka et al. 2016; Sivalingam et al. 2019). Most of the antibiotics isolated from *Streptomycetes* act as inhibitors of protein synthesis, while some disrupt cell wall biosynthesis or integrity of cell membrane (Walsh and Wencewicz 2014; Louzoun Zada et al. 2018). There are also some antibiotics which induce the defense mechanism of host plants. Some bioactive natural products act on the protein coat of viruses, while some induce tolerance to plant against pathogen (Gupta and Birdi 2017; Köhl et al. 2019). In Canada, European Union, and the United States, uses of antibiotics in controlling plant disease are strictly prohibited (Kumar et al. 2019).

Species of the genus *Streptomyces* are also reported to produce proteins and peptides (blasticidin, mildiomycin, and polyoxins) which are used as a defense against pathogen (Sathya et al. 2017; Harir et al. 2018). Only few antimicrobial peptides have been registered and commercialized to protect crops because they can easily oxidize and hydrolyze and have less physical and chemical stability (Rai et al. 2016; Kumar et al. 2018). Antimicrobial peptides are used to develop various infection control agents and also used in cancer and diabetes treatment (Pfaltzgraff et al. 2018). Bacteriocins are reported to control spoilage and foodborne pathogens (Da Costa et al. 2019).

The extracts or metabolites isolated from microorganisms can be used as crude extracts, antibiotics, harpin, and proteins that prevent or reduce the diseases (Harish et al. 2008; Cheesman et al. 2017). Harpin is a heat-stable and glycine-rich protein, produced by pest *Erwinia amylovora*, which is effective against various pests on different hosts (Li et al. 2010; Zhou et al. 2019). Harpin is also reported to be effective against fungal pathogens during postharvesting (Alkan and Fortes 2015). It is also reported for accelerated growth, enhancing germination and flowering, stimulation of resistant responses, etc. (Yuan et al. 2017; Lymperopoulos et al. 2018). Four active regions have been reported in molecule of harpin, that is, HrpW (source: *E. amylovora*), HrpN (source: *E. amylovora*), PopA (source: *Ralstonia solanacearum*), and HrpZ (source: *Pseudomonas syringae*) (Kim and Beer 1998; Jin et al. 2001). These active regions are reported to likely increase the efficacy in growth stimulation and various other processes (Kurutas 2016). Another bioactive product, yeast extract hydrolysate, was reported to be isolated from *Saccharomyces cerevisiae* that also induces tolerance responses. Strobilurin isolated from fungus *Strobilurus tenacellus* is reported to the electron transport chain by binding with Qo site of cytochrome b (Ding et al. 2008; Song et al. 2015). Seventeen fungicides derived from strobilurin and its derivatives are commercialized (Bartlett et al. 2002).

2.2.2 Plant-Derived Natural Products

From earlier times, plant and plant-derived products have been used as good source of bioactive compounds (Amit Koparde et al. 2019). Various plant extracts, leaves, stems, and even roots are reported worldwide not only as medicines but also as biopesticides (Koma 2012).

Five families of the plant kingdom, Apocynaceae, Flacourtiaceae, Fabaceae, Lamiaceae, and Asteraceae, are reported as potent sources of biopesticides and bioactive natural products (Gakuya et al. 2013; Céspedes et al. 2014). To facilitate the development of biopesticides from plant sources, the extraction processes should be standardized, plant material should grow under natural conditions, and plant products should not affect nontarget species (Grzywacz et al. 2014; Tembo et al. 2018). Peels of pomegranate and citrus fruits and pomace from olives and grapes are also reported to inhibit various pathogens (Fourati et al. 2019).

The resins of conifers are also used against microbial pathogens and are good source of bioactive natural products (Termentzi et al. 2011; Gouda et al. 2016). Advancement in tissue culture techniques aids in the development of cell cultures of various plants to accelerate the production of bioactive natural products (Hussain et al. 2012; Cardoso et al. 2019). Salicylic acid and its derivatives isolated from *Reynoutria sachalinensis* of family Polygonaceae were also reported to have resistance to phytopathogens and play an important role in acquiring systemic resistance (Paul and Sharma 2002). It is phytotoxic in nature and used as preventative, trunk injection, seed treatment, and as anti-infectious agent (Lin et al. 2009). Salicylic acid also reduces size of lesion and virus titers (Park et al. 2009; Künstler et al. 2019). Anthraquinone compound isolated from extract of knotweed contains terpene in their functional group which is reported to act against phytopathogens and induce defense response of plants (Shan et al. 2008). Simple phenolics (salicylates) act as antifeedant to insect herbivores such as *Operophtera brumata* (L.) in *Salix* leaves, and there is a negative correlation between the salicylate levels and the larval growth; however, salicylic acid (SA) is much more important as phytohormone than as deterrent (War et al. 2012).

Biopesticides are also reported to be isolated from *Lupinus albus doce* of family Fabaceae (Gwinn 2018). It has a BLAD oligomer having chitinolytic and lectin-binding activities (Ruiz-López et al. 2010). It is friendly to honey bees and protects protein of legumes from allergic responses (Lucas et al. 2009). Alkaloids and benzophenanthridine alkaloids were also reported to be isolated from extracts of *Macleaya cordata* (family: Papaveraceae) which is effective against *Erysiphe graminis* and *Botrytis cinerea* (Kosina et al. 2010; Yu et al. 2014; Ge et al. 2015).

Phenolic compounds contribute to host plant resistance against insects and herbivores (Fürstenberg-Hägg et al. 2013). They are also reported to act as defensive mechanism against weeds, microbial infections, and herbivores (Kortbeek et al. 2019). Lignin, a phenolic heteropolymer, plays a central role in plant defense against insects and pathogens (Barakat et al. 2010). Phenols also play an important role in cyclic reduction of reactive oxygen species (ROS) such as superoxide anion and hydroxide radicals, H_2O_2, and singlet oxygen, which in turn activate a cascade of reactions leading to the activation of defensive enzymes. It limits the entry of pathogens by blocking it physically or increasing the leaf toughness that reduces the feeding by herbivores and also decreases the nutritional content of the leaf (Sharma et al. 2012; Nita and Grzybowski 2016). Lignin synthesis induced by herbivory or pathogen attack and its rapid deposition reduce further growth of the pathogen or herbivore fecundity (Miedes et al. 2014; Xie et al. 2018). Oxidation of phenols catalyzed by polyphenol oxidase (PPO) and peroxidase (POD) is a potential defense mechanism in plants against herbivorous insects. Quinones formed by oxidation of phenols bind covalently to leaf proteins and inhibit the protein digestion in herbivores (Felton and Gatehouse 1996; Haruta et al. 2001). In addition, quinones also exhibit direct toxicity to insects (Sugumaran and Bolton 1995). Alkylation of amino acids reduces the nutritional value of plant proteins for insects, which in turn negatively affects insect growth and development (Chen et al. 2005; Zhao et al. 2019). Plants are also reported to produce flavonoids which protect the plant against insect pests by influencing the behavior, growth, and development of insects (Mierziak et al. 2014). Tannins are also reported to act on phytophagous insects by affecting the growth of phytopathogens. They bind with proteins and midgut lesions and reduce the nutritional absorption efficiency of phytophagous insects (Barbehenn and Peter Constabel 2011; Vandenborre et al. 2011; Martinez et al. 2016). Various bioactive compounds isolated from plant sources are represented in Fig. 2.3.

Flavonoids contain anthocyanins, flavones, flavonols, flavanones, dihydroflavonols, chalcones, aurones, flavan, and proanthocyanidins (Iwashina 2000). More than 5000 flavonoids have been reported in plants (Hossain et al. 2016). Flavones such as flavonols, flavones, proanthocyanidins, flavan-3-ols, flavonones, flavans, and isoflavonoids function as feeding deterrents against many insect pests (Mierziak et al.

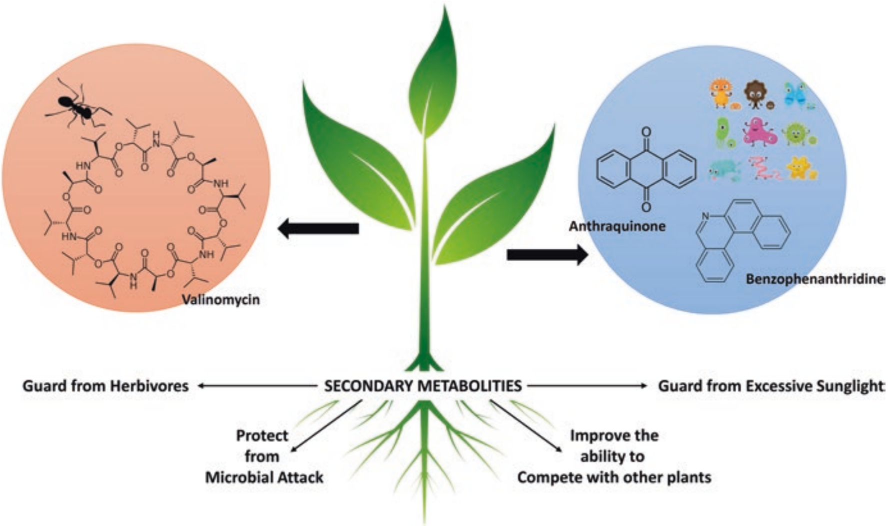

Fig. 2.3 Various bioactive compounds isolated from plant sources as defense for plant diseases

2014; Panche et al. 2016). Flavonoids such as flavones 5-hydroxyisoderricin, 7-methoxy-8-(3-methylbutadienyl)-flavanone, and 5-methoxyisoronchocarpin isolated from *Tephrosia villosa* (L.), *T. purpurea* (L.), and *T. vogelii* Hook, respectively, function as feeding deterrents against *Spodoptera exempta* (Walk.) and *Spodoptera littoralis* (Bios) (Chen et al. 2014; Samuel et al. 2019). Angustone A, licoisoflavone B, angustone B, angustone C, isoflavones, licoisoflavone A, luteone, licoisoflavone B, and wighteone are feeding deterrents to insects and also have antifungal activity against *Colletotrichum gloeosporioides* (Penz.) and *Cladosporium cladosporioides* (Fres.) (Wang et al. 2013).

Essential oils isolated from plant sources are used as treatment of various diseases in vegetables and fruits. They are either used singly or with other products as edible coating or film (Sánchez-González et al. 2011; Ju et al. 2019). These oils are major component for formulation of biopesticides which include *Allium sativum* (garlic, family *Amaryllidaceae*), *Syzygium aromaticum* (clove, family Myrtaceae), *Cinnamon cassia* and *Cinnamomum zeylanicum* (cinnamon of family Lauraceae), *Mentha piperita,* and *Thymus vulgaris* (peppermint and thyme of family Lamiaceae) (Pohlit et al. 2011). These essential oils are mixture of phenols and terpenes (Dhifi et al. 2016; Morsy 2017). The active component in thyme oil is thymol, menthol in peppermint, methyl eugenol in clove oil, cinnamaldehyde in cinnamon oil, and sulfur compounds in garlic oils (Nazzaro et al. 2013). Thyme oil is used to control cucurbit disease and bacterial spot in turnip (Sivakumar and Bautista-Baños 2014). Garlic is reported to be effective against *Alternaria* blight on mustard. Clove oil is used to control fungal infections (Liu et al. 2017).

Bioactive oil isolated from *Simmondsia chinensis* species of Simmondsiaceae family and is enriched in wax esters, which is primarily used to block the oxygen uptake of mycelium (Perez-Rosales et al. 2018). Hydrophobic and azadirachtin extract of oil isolated from *Azadirachta indica* (neem) is reported to act as biocidal agents with disrupts normal growth of pests. It also inhibited the growth of *Chaetomium globosum* (soft wood fungus) (Selim et al. 2014; Fatima et al. 2016). To control early blight of tomato, cotton seed oil isolated from *Gossypium hirsutum* of family Malvaceae was used which act as growth inhibitor of bacterial infections. Oil of species *Chenopodium ambrosioides* of family Chenopodiaceae is a renowned antihelminthic which protects storage foods from microbial attack (Naqvi et al. 2017). Oils contains carvacrol or ascaridole which are used to control nematodes and soilborne fungi (Oka et al. 2000). Oil of tea plants is enriched in terpenes and terpinenic which were having antimicrobial activities and also used as biopesticides against viruses and plant fungal infections by infecting membrane integrity (Guimarães et al. 2019). Oils isolated from barley (*Blumeria graminis*) are used as plant protection agents and as fungicides. Isoflavonoids (judaicin, judaicin-7-*O*-glucoside, 2-methoxyjudaicin, and maackiain) isolated from the wild relatives of chickpea act as antifeedant against *Helicoverpa armigera* (Hubner) at 100 ppm (Simmonds and Stevenson 2001). Judaicin and maackiain are deterrent to *S. littoralis* and *S. frugiperda,* respectively. Cyanopropenyl glycoside and alliarinoside strongly inhibit feeding by the native American butterfly, *Pieris napi oleracea* L., while a flavone glycoside, isovitexin-6″-β-D-glucopyranoside, acts as a direct feeding deterrent to the late instars (Anthoni et al. 2001).

2.2.3 Algal-Derived Natural Products

Biofuels obtained from algal bodies are also used as biopesticides as they hinder various metabolic processes and enzyme activity of pathogens (Hannon et al. 2010; Costa et al. 2019). Laminarin is another bioactive natural product isolated from brown algae which is used for preserving food items (Kadam et al. 2015; Ciko et al. 2018). It is an oligosaccharide having mannitol or glucose chain in its terminal position. The chains are composed of b(1,6) branches and b-(1,3)-D-glucans (Legentil et al. 2015). Laminarin is a well-known biopesticide, but it also acts as bio-stimulant. Saponins are isolated from *C. quinoa* that are reported to suppress various plant diseases (Yoon et al. 2013; Kregiel et al. 2017). They act as fungicides and resistance inducers, and have low mammalian toxicity (Dias 2012; Thakur and Sohal 2013; Lamichhane et al. 2018).

2.2.4 Marine-Derived Natural Products

Most of the marine-derived natural products are potent source of bioactive compounds which act to treat different ailments (Nair et al. 2015).The first bioactive compounds were reported in the 1950s which were isolated from *Cryptotheca crypta* (Caribbean sponge) that includes *spongothymidine* and *spongouridine* (Ruiz-Torres et al. 2017). These two compounds were reported as potent antiviral and anticancer agents. Other bioactive products like *discodermolide* isolated from

Discodermia dissoluta are reported to having strong anticancer activity (Khalifa et al. 2019; Ha et al. 2019). Microalgal species contain various bioactive compounds which are oleic acid, palmitoleic acid, linolenic acid, cyanovirin, vitamins E and B12, β-carotene, lutein, zeaxanthin, and phycocyanin functional groups which act as various antimicrobial agents having potential to prevent the diseases (De Morais et al. 2015; Jena and Subudhi 2019). Algal bodies contain heterocysts which fix atmospheric nitrogen and induce plant growth by synthesizing amino acids (Issa et al. 2014; Magnuson 2019).

2.3 Conclusion and Future Prospects

Disease control of plants is often regulated by chemical fertilizers and pesticides. These chemicals not only kill the pests but also increase the production of crops. However, all these chemical agents are hazardous to both aquatic and terrestrial ecosystems; besides this, various pest species have developed tolerance to wide range of these pesticides, insecticides, fungicides, etc. Bioactive compounds isolated from various sources have defense mechanisms against various stress and microbial pathogens. Various compounds isolated from plant sources, algal sources, microbial sources, marine sources, etc., act as elicitors for plant defense against various sources. These include chitosan, salicylic acid, benzoic acid, benzothiadiazole, alkaloids, flavonoids, terpenes, proteins, peptides, blasticidin, mildiomycin, polyoxins, and phenolic compounds which act against various plant diseases caused by bacteria, fungi, and viruses. Formulations of bioactive natural products are critical to overcome agricultural challenges such as being nutritious, safe, and adequate for supply to all human populations. These bioactive compounds minimize the use of chemical agents and contribute to eco-friendly sustainable agriculture practices.

Development of new gene cassettes using metabolic engineering into these sources will not only increase the efficiency of these bioactive compounds but also help in the production of secondary metabolites which act as valuable defense system.

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