# 1 Natural Metabolites: An Eco-friendly Approach to Manage Plant Diseases and for Better Agriculture Farming

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**Abstract**

Natural metabolites and biocontrol agents are becoming more popular and are getting consideration to be viable replacement methods for controlling various plant diseases nowadays because the environment is safer and, in some cases, the only option is available for the protection of plants against the pathogens. In the present scenario, beyond good horticultural and agricultural practices, producers often depend mostly on chemically synthetic pesticides and fertilizers that are not only harmful but also very costly. Development of pathogen-resistant breeds becomes a worldwide problem which imposes and threatens some chemical companies to produce new pesticides with their registration process and profitability. There has been a considerable change in the perspective of farmers toward the use of pesticides for crop protection and crop production. There are several types of biological control agents and natural metabolite products are available, but for effective acquisition and future development, it will need a great understanding of complex interactions between humans, plants, and the environment. In this chapter, we will discuss wide varieties of plants and

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J. Singh, A. N. Yadav (eds.), *Natural Bioactive Products in Sustainable Agriculture*, https://doi.org/10.1007/978-981-15-3024-1_1

pathogens and their interaction and management through natural metabolites produced by microbes and plants. These interactions can affect the health of plants in several ways. There are several microbes that reside in plant roots and interact with plants that are beneficial while some can be harmful because they are involved in the development of plant diseases, which occur at various levels of interaction scale that leads to natural control.

**Keywords**
Biocontrol · Natural · Metabolites · Plant health · Plant pathogens

## 1.1 Introduction

Agriculture is one of the most growing fields, which include many crops, that might be affected by various abiotic and biotic stresses. Biotic stresses include bacteria, fungi, viruses, insects, nematodes, and weeds, which affect in different developmental stages. The decreased production of a new crop cultivar is the result of biotic stress (Sanjay and Tiku 2009).

There are so many types of plant diseases that may include reduced quantity and quality of crop, threat to environment and human health, increased cost of production, less remunerative alternatives, and deterioration of natural resources (Eilenberg et al. 2001). After seeing the present scenario, there are many varieties of natural metabolites produced by biocontrol agents that are available. In numerous decade ago, biological metabolites are used for the control of various plant diseases. So, the purpose of living microbes to control the growth of plant pathogen is an important part of success (Kumar and Saxena 2009). Thus, it is a challenging task to overcome the damage caused by plant pathogens. It is compulsory to devise strategies to combat these problems. Although there are multiple pesticides, biocontrols or chemicals are available in the market, but to reduce the growth of plant pathogens, these compounds may have certain drawbacks; for example, the little amount of these compounds present in fruits or grains could harm human being and may be harmful to the environment, which can cause water and soil pollution, animal and food contamination, and beneficial microbe elimination. Keeping in view the hazardous effect of pesticides, natural products seem to be an eco-friendly approach to manage the disease and reduce the toxic effects of pesticides and fungicides to environment and human health.

## 1.2 Role of Natural Plant Products in Disease Management

The accessibility of nutritious and safe food could be increased by increasing the sustainability of agricultural production system, which is the global challenge for food security. The use of bioactive natural products isolated from natural products for plant protection and sustainability may be incorporated in plant production. In modern agriculture, the use of botanical and microbial natural products may lead to the development of natural inducers and antimicrobial agents of plant host defense system. In much previous research, there are so many plants, such as neem, citrus, garlic, moringa, etc., which have been used for the management of several bacterial and fungal diseases. On chemical basis, many plant metabolites act as antifungal agents like flavones, flavonoids, quinines, tannins, terpenes, and saponins. All these always played important role as antifungal agents. These are all produced by plants against microbial infections and found to be effective substances against harmful microorganisms and pathogens (Ciocan and Bara 2007). Flavonoids are allelopathic compounds, phytoalexins, and antimicrobial and detoxifying agents that always act as signal molecules and as protector from various stresses. Flavonoids also play an important role in abiotic stresses like temperature and drought tolerance, frost hardiness, and freezing tolerance (Iwashina 2003).

Isoflavonoids are involved in the defense mechanism against plant pathogen, and these can be characterized by migration of phenyl ring. In species *Mangifera indica*, the major phytoalexin is vestitol, belonging to class isoflavones (Lanot and Morris 2005). In several previous kinds of researches, scientist investigated the presence of flavonoid phytoalexins in cucumber and reported that silicon is involved in the defense mechanism against fungal proteins (Fawe et al. 2001). Flavonoids function as detoxifying agents, justified by flavonoid peroxidase that plays an important role in $H_2O_2$ scavenging (Yamasaki et al. 1997). Flavonoids are not only able to detoxify the reactive oxygen species but also chelate with heavy metals, resulting in divergence of molecular structures. Flavonoids also play an important role against plant viruses. Galangin (3,5,7-trihydroxyflavone), a flavonoid isolated from *Helichrysum aureonitens*, creates the defense mechanism against the viruses and gram-negative bacteria and fungi (Cowan 1999).

### 1.2.1 Coumarins

Coumarin is a colorless, crystalline solid that is bitter in taste. It was first screened from tonka beans in 1820 by A. Vogel (Munich). Basically, coumarins are phenolic substances containing various secondary metabolites, composed of pyrone rings and fused benzene. Coumarins are inducible antifungal chemicals that function as antifungal agents. Many coumarins, like scopolin, scopoletin, and umbelliferone, are formed in tissues of plant in response to fungus like *Fusarium oxysporum*, which attack potato roots. When roots of parsnip and celery were inoculated to *Sclerotinia sclerotiorum*, the level of furanocoumarins was decreased (Rahman 2000). Coumarins are also known as phytoalexin, and in much previous study, it was reported as antifungal agents that develop the defense mechanism against fungal bodies (Brooker et al. 2007). In few works, it was also regarded as antibacterial and anti-insecticidal agents. It has antibacterial effects on animal and pathogenic bacteria (Razavi et al. 2009). In other previous studies, coumarin and murraxocin acts as strong insecticidal agents having mortality on larva and eggs of insects (Sharma et al. 2006). Coumarin is also reported to act as an ovicide agent (Tasleem et al. 2012). There are many agents like carbazole derivatives; clausenidin, dentatin, and clauszoline extracted from *Clausena excavate* exhibit antimycotic activity. In several in vitro studies, coumarins showed antibacterial and antifungal activities (Nakajima and Kawazu 1980). Synthetic coumarins and angelicin derivatives were found effective against *A. niger*, *C. albicans*, *S. cerevisiae*, and *C. neoformans.*

### 1.2.2 Tannins or Gallotannin

Tannin is a polyphenolic biomolecule and is responsible for the flavoring and astringency in tea. Normally, tannin is found in the bark, wood, roots, leaves, and fruits of plants. The molecular weight of tannin ranges from 500 to 3000 kDa, and it is divided into two categories: (i) hydrolysable and (ii) condensed tannins. Hydrolyzable tannins are derived from flavonoid monomers and produce ellagic or gallic acids upon heating with sulfuric and hydrochloric acids. Hydrolyzable tannins are extracted from vegetable plants such as oak wood (*Quercus petraea*, *Quercus alba*, and *Quercus robur*), chestnut wood (*Castanea sativa*), tara pods (*Caesalpinia spinosa*), myrobalan, and gallnut. There is a carbohydrate, usually D-glucose, in the center of tannin molecule as multiple esters. Certain examples of tannins are gallic acids, which are esters of glucose found in leaves and bark of many plants. They are also formed by the condensation reaction of flavan derivatives (Tasleem et al. 2012). The examples of condensed tannins are polyflavonoid tannins, proanthocyanidins, pyrocatecollic-type tannins, catechol-type tannins, etc., formed by condensation of flavans. Condensed tannin is also found in grape, commonly called as procyanidins, consisting of 2–50 polymer (or more) catechin units linked by carbon-carbon bonds. Tannins create the defense mechanisms by the binding of dietary proteins of digestive enzymes. Many types of tannin act as insecticidal agents and could have a negative effect on insects because they were having basic gut pH and tannins don't act on those proteins (Barbehenn and Constabel 2011).

### 1.2.3 Alkaloids

Alkaloids usually contain more than nitrogen atoms in their heterocyclic ring. These compounds were having weak and neutral acidic properties (Manske 1965; Lewis 1998). The function of alkaloids in the plant is uncertain. There is no such importance of alkaloids, although they are regarded only as by-products of plant metabolism. Sometimes, they may act as reservoirs for protein synthesis. In previous research, it was reported that generally alkaloids are therapeutically significant plant substances (Tasleem et al. 2012). Alkaloids are produced by large group of various organisms like plant fungi, animals, and bacteria (Roberts 1998). Alkaloids have antimalarial, antibacterial, analgesic, and anticancer properties. The first reported alkaloid was morphine, derived from *Papaver somniferum* (opium poppy) in 1805.

The alkaloid like 2-(3-4-dimethyl-2-5-dihydro1H-pyrrol-2-yl)-1-methylethylpentanoate derived from *Datura* shows antifungal activities against *Candida* and *Aspergillus* species. Fragulanine is a cyclic peptide quinoline alkaloid isolated from *Melochia odorata* that showed antifungal activity against the pathogenic fungi. Other alkaloid, 3-methoxysampangine, derived from *Cleistopholis patens* were reported to have antifungal activity against *C. neoformans*, *C. albicans*, and *A. fumigatus*. N-Desmethylcycleanine, cycleanine, and cocsoline from *Albertisia villosa* are the antifungal alkaloids that were reported from higher plants (Tasleem et al. 2012).

### 1.2.4 Terpenoids

Terpenoids are commonly called as isoprenoids. Basically, these are the assorted class isolated from terpenes. Terpenes are large and diverse class of hydrocarbons produced by varieties of plants. They have strong odor and may protect the plants by deterring herbivores and by parasites of herbivores. Terpenoids act as antioxidants and execute various functions in plants and animals (e.g., carotenoids function as essential pigments for light extracting and provide photo protection and plant pigmentation). Plant terpenoids are used as herbal remedies against various pathogens and diseases. Terpenoids give odor to eucalyptus, flavors to ginger cinnamon and cloves, red color in tomatoes, and the yellow pigmentation in sunflowers (Specter 2009). Terpenes (diterpenes, triterpenes, tetraterpenes, hemiterpenes, and sesquiterpenes (C15)) contain oxygen in their side chain and are termed as terpenoids. Some common examples are artemisinin (sesquiterpenoids), farnesol, camphor (monoterpenes), and methanol.

In several research studies, it was reported that terpenes or terpenoids work against bacteria, viruses, and protozoa. Capsaicin enhances the growth and development of *Candida albicans*, which inhibit the growth of various types of bacteria (Cowan 1999). Terpenes are also considered as antifungal agents. Monoterpenoids are involved in the innate immunity against various plant pathogens. The major components of oils, that is, 1,8-cineole, p-cymene cineole, carvacrol, thymol, and geranial, exhibit antifungal activity. The extracts from *Agastache rugosa* (essential oil) were reported to have antifungal activity. The essential oil extracts from the leaves of *Litsea cubeba* contain n-transnerolidol 3, 7-dimethyl-1, 6-octadien-3-ol, and cis-ocimene that manifest antifungal activities. Tri-terpenoid glycosides obtained from *Bellis perennis* and *Solidago virgaurea* inhibit the growth and development of human pathogenic yeasts (*Cryptococcus* and *Candida* species) (Tasleem et al. 2012).

## 1.3 Plant Growth-Promoting Rhizobacteria (PGPR)

The root system of the plant system is surrounded by a narrow zone of soil called rhizosphere (Walker et al. 2003). The bacterial community colonizing this narrow environmental zone is term as “rhizobacteria” (Kloepper et al. 1991). The bacterial communities that colonize the roots of the plant and support their growths are called plant growth-promoting rhizobacteria (PGPR) (Beneduzi et al. 2012). These bacteria are one of the most effective and eco-friendly methods for the management of plant disease (Compant et al. 2005). PGPR as biocontrol agents have several benefits over chemical practices, because PGPR are nontoxic and they are naturally occurring microorganism having endurable applications.

The application of PGPR as a cost-effective control method of pest management in roots has been reported by several workers (Lucy et al. 2005; Whipps 2001). Different bacterial strains have shown to have ability for development as biocontrol agents on cereals. Bacterial isolates from the plant root, such as *Bacillus*, *Pseudomonas*, and *Azotobacter*, showed antagonistic activity to check the plant pathogen and act as disease management agent (Berg and Smalla 2009).

The biocontrol potential of *Pseudomonas* sp. and *Bacillus* spp. as important biocontrol agents to strive against root and soilborne microbial pathogens has been reported in several crops like wheat, tomato, potato and chickpea (Hussain and Khan 2020; Dashti et al. 2012; Perez-Montano et al. 2014). Several species of *Bacillus* such as *B. licheniformis*, *B. cereus*, *and B. thuringiensis* were reported to be potential biocontrol agents. *Bacillus* spp. screened from the chickpea rhizosphere have shown to reduce the pathogenic activity of fungus called *Fusarium oxysporum*, which is reported to cause *Fusarium* wilt disease. In a greenhouse experiments, *Bacillus* strains that was isolated and reported from the sorghum rhizosphere in Ethiopia and wild grass sp. in South Africa have antagonistic affects against the root rot disease caused by *F. oxysporum* and crown rot pathogens by *Pythium ultimum* (Idris et al. 2007).

The plant growth-promoting rhizobacteria exerted different mechanisms such as antibiosis, secreting toxin surface compound (bio-surfactants) and volatiles, chitinase cell wall-degrading enzymes, and α-1,3-glucanase and also induce systemic resistance in plants to deplete the soilborne pathogens (Perez-Montano et al. 2014; Haas and Défago 2005; Compant et al. 2005; Van Loon 2007, Whipps 2001). The earlier reported mechanism of biocontrol is the secretion of siderophore ligands that efficiently confiscate iron and inhibit the growth of pathogen (Raaijmakers et al. 2002).

## 1.4 Fungi as Biocontrol Agents

Nowadays, fungi biological control is considered to be a rapid and effective developing natural phenomenon with wide applications in industrial sector like food production and food yield. Harman et al. (2013) reported that *Trichoderma* species allows for the development of biocontrol strategies against economically important plant pathogen. Antagonistic effect of *Trichoderma* spp. is due to the secretion of secondary metabolites against *Pythium ultimum* and *Rhizoctonia solani* (Harman et al. 2004). Several other fungi like *Pochonia chlamydosporia* isolates have been evaluated as biocontrol agents against the root-knot nematodes (RKN) with different crops and experimental conditions (Shurf et al. 2014). Endophytic colonization of the root by *P. chlamydosporia* suppresses the growth of the pathogens and enhances the growth and development of the plant (Maciá-Vicente et al. 2009)

## 1.5 Role of Mycorrhizae in Disease Management

To develop effective and durable protection to root system, the role of mycorrhiza against pathogenic population is well established (Thakur et al. 2005). Mycorrhizal fungi are most common fungal association with roots of majority of plants.

The mycorrhiza (fungus root) is defined as an association between fungi and plants that establishes on tissue of root system during the time of active plant growth and makes unfavorable environment for pathogens. Mycorrhizal fungus acts as biocontrol agent against various plant pathogens, which is a relatively new and eco-friendly technique. Several studies have proved that tree seedlings with mycorrhizal associations exhibit more resistance to feeder roots against pathogenic fungi/bacteria/nematodes than non-mycorrhizal roots (Al-Karaki 2000).

Ectomycorrhizae multiply on the root surface producing a netlike structure called the Hartig net. They reduce the development of disease by exerting different mechanisms including antibiosis, by synthesizing antifungal compound and developing a barrier around the root of the plant (Duchesne 1994). Root rot disease of red pine caused by *F. oxysporum* and *F. moniliforme* is effectively controlled by ectomycorrhizal fungi like *Paxillus involutus*.

Vesicular arbuscular mycorrhizae (VAM) are another significant part of the microbial soil community that provide vital benefit for plant growth (Sukhada et al. 2010; Yinsuo et al. 2004). The VAM fungi are not only beneficial for plant development, but it also develop the resistance in the host plant against various soilborne plant pathogens (Ziedan et al. 2011; Upadhyaya et al. 2000). Among the VAM fungi, the genus *Glomus* is very common with species like *G. fasciculatum*, *G. mosseae*, *G. constrictum*, *G. monosporum*, and *G. macrosporum.* During the establishment on the root system, they prevent root infections by reducing the entry sites of pathogens and encouraging host defense. They have also been found to decrease the infection of root-knot nematode in different plant systems (Linderman 1994). The effect of *Pseudomonas syringae* on tomato is significantly decreased when the host plants are inoculated with mycorrhizae fungi (García-Garrido and Ocampo 2002). The mode of action involved in these interactions includes indirect effects, chemical interactions, and physical protection (Fitter and Garbaye 1994). The other strategy adopted by VAM fungi includes improved nutrition in the plant; increase lignification on the root system; and chemical composition of antifungal isoflavonoids, chitinase, etc. (Morris and Ward 1992).

Arbuscular mycorrhizal fungi (AMF) are reported to manage a number of crop diseases, especially root diseases (Xavier and Boyetchko 2004). They can affect the pathogens and suppress the diseases through the development of systemic resistance in the host (Jung et al. 2012; Pozo and Azcon-Aguilar 2007; Pineda et al. 2010). It has been found that mycorrhizal induce resistance (MIR) is the result of active depletion of components in the Salicylic acid (SA)-dependent defense pathway, which causes systemic priming of jasmonic acid-dependent defenses (Pozo and Azcon-Aguilar 2007; Hause et al. 2007).

## 1.6 Management of Plant Diseases Caused by Plant Parasitic Nematodes

Agriculture production in India has sustained losses of millions of dollars due to various factors. Among them, one of the major constraints is pest diseases, which are the limiting factor in the cultivation of crops. Among them, diseases caused by plant parasitic nematodes (PPN) are one of the constraints in reducing both the quality and yield of the crops. They cause 21.3% crop losses amounting to ₹102039.79 million ($1577 million) annually; the losses in 19 horticultural crops were assessed at ₹50224.98 million, while for 11 field crops it was estimated at ₹51814.81 million. Rice-rot nematode *Meloidogyne graminicola* was economically most important causing yield loss of ₹23272.32 million in rice. Citrus (₹9828.22 million) and banana (₹9710.46 million) among fruit crop and tomato (₹6035.2 million), brinjal (₹3499.12 million), and okra (₹2480.86 million) among the vegetable crops suffered comparatively more losses (Walia and Chakrabarty 2018; Khan et al. 2010). It has been estimated that overall losses amount to $78 billion globally due to RKN (Chen et al. 2004).

Plant parasitic nematodes are regarded as biggest enemy of crops due to their small size and natural habitats where they established a feeding site. They lead major structural changes in root system and metabolism. Root-knot nematodes (RKN), such as *Meloidogyne* spp., are the most dangerous nematodes worldwide. They act on more than 5000 plant species and cause economic losses in many horticultural and agricultural crops (Ntalli et al. 2010).

One or more nematode pests are always associated with every crop, which cause economic loss to crop, and their control is the major requirements for increasing the crop productivity. Pesticides are currently being used to manage these nematode pests leading to environmental and health concerns and resulting into the suppression of other naturally occurring biocontrol agents as well as resistance in their nematodes.

Many soil-inhabiting microorganisms, such as fungi, bacteria, protozoans, viruses, turbellarians, enchytraeids, mites, predatory nematodes, collembolans, and tardigrades, are parasites, predators, or antagonistic to plant parasitic nematodes. These microorganisms have been exploited as biocontrol agents for the management of PPN in several agricultural and horticultural crops. The increasing thrust toward sustainable agriculture and integrated pest management has led to biological control emerging from their status as a fringe sector to being viewed as an intrinsic part of crop protection. A brief description on the most promising organisms is furnished below.

### 1.6.1 *Paecilomyces lilacinus*

This is an opportunistic fungus prevalent in many soils. This fungus parasitizes the egg of root-knot nematodes and suppresses nematode hatching. Inoculation of this fungus at root zone could significantly reduce root loss due to nematode infestation and improve plant growth.

### 1.6.2 *Trichoderma* spp.

These are hypomycetous fungi widely used against several disease-causing fungi. Several species of *Trichoderma* colonize egg masses of nematodes. Although direct parasitization was not observed with any of these isolates, distortion of nematode eggs was frequently seen with *T. harzianum* and *T. viride*. Culture of these isolates showed antagonistic effect against nematodes. *T. harzianum* suppress root knot nematodes and improve growth of the plant.

### 1.6.3 *Pochonia chlamydosporia*

This fungus is known as biocontrol agent of root knot and cyst nematodes. Isolate of this fungus parasitizes root-knot nematode eggs and suppresses their hatching by more than 55% within 24 h. It is a promising biocontrol agent to controlled nematode problem and significantly increased yield.

### 1.6.4 Mycorrhizal Fungi

These fungi are obligate dependents on plants for nourishment. Their symbiotic association with roots increases the plant's ability to absorb water, phosphorus, and other elements. Mycorrhizae are known to increase host tolerance against nematode infestation due to enhanced "P" status of the host between fungus and the nematode. Significant increase in growth of plant and reduction in the root knot nematode populations were observed when challenged with such fungi like *Glomus mosseae*, *G. fasciculatum*, *Acaulospora laevis*, and *Gigaspora margarita.*

### 1.6.5 *Pasteuria penetrans*

This bacterium inoculation reduced nematode population and thereby improved the vegetative growth of the plants. However, mass multiplication of this bacterium is yet to be standardized.

### 1.6.6 *Pseudomonas fluorescens*

*P. fluorescens* is a rhizosphere bacterium, which is commonly found in soils. This bacterium is quite popular among the farmers to control fungal diseases. Some of the isolates of this bacterium possess inhibitory effect on nematode and enhance root growth.

### 1.6.7 Endophytic Bacteria

Endophytic bacteria like *Pseudomonas aeruginosa*, *Bacillus megaterium*, and *Curtobacterium luteum* offer excellent nematicidal properties. Their endophytic nature is an added advantage for effectively preventing the nematode entry into roots.

### 1.6.8 Entomopathogenic Nematodes

Entomopathogenic nematodes (EPNs) are emerging as a potent biocontrol agents. They have a great potential as biological control agents because they have wide host range, are easy to handle, have short life cycle, are economically produced at large scale, and are environmentally safe. They are symbiotically associated with bacteria, which played a significant role in suppressing nematode population.

## 1.7 Future Prospects

In the present scenario of crop production, the natural metabolites produced by biocontrol are of utmost importance; however, its application needs to be fully exploited. The research in this area is still confined to the laboratory, and very little attention has been given to produce the profit-making formulations of the bioagents. Moreover, cost-effective products have not been used conveniently by the farmers owing to the limited available information regarding its use. Therefore, to popularize the concept of biological control extension at basic research levels in this direction needs to be improved.

Most bioagents fail to perform infield trial experiments but perform well in the laboratory conditions. There are many reasons out of which probably blame to the ecological and physiological constraints that limit the efficacy of metabolites. To improve the selection and characterization of metabolites, biotechnology and other molecular tools are gaining importance to potentially solve the problem in near future. Increasing the efficacy of BCA, different methods such as mutation or protoplasm fusion could be a good idea. To better understand the mechanism of bioagents and to evaluate their environmental factors that favor the hasty growth of biological agents, there is an urgent need of efficient bioagents in cost-effective manner for market entrance.

## 1.8 Conclusion

There are currently more than 30 bacterial and fungal products for the management of soilborne diseases of agricultural crops. In the recent era, in India, there is a new progressive research and development (on applied level) on new biological agents at field levels that have find a new place on active application to disease-infected parts of the crops, but other problems have also emerged, which are new obstacle in the development of biological agents like lack of constancy on its effectiveness. When these biological agents are applied to control the diseases, they show some inconsistency or they are less effective at ground/base level, which may be due to that before any integration between abiotic and biotic factors that can provide and help to increase the efficacy of biocontrol activity. Biological agents are more valuable section of integrated pest management systems; while using other types of pest management strategies like chemical, mechanical, and organic, there should be more coordination between each other. Nowadays, people are highly aware of organic production and are very interested and active in participating in activities likes home gardening and terrace farming in urban populations and cities, as well as reducing the usages of harmful pesticides, fungicides, and insecticides, which are creating a market of the natural metabolite products. Probably, in spite of these metabolites, more improvement can be done on isolation, formulation, and their application processes, especially at farmer's field level. The twenty-first century will be the age of biotechnology that will contribute an important role in the field of plant pathology and lead to the development of new strategies for natural metabolites.

**Conflict of Interest** The authors declare that they have no conflict of interest.

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