

Trichoderma role as an essential plant growth promotion-a review



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Summary

In the world, pest infestation is responsible for 70% or more of per cent losses in agricultural productivity, and mycopesticide can provide an alternative option to pest control option as an alternative to synthetic pesticides. *Trichoderma* is a genus of fungal species, and *Trichoderma viride* is one of the known fungal species in categories that exhibit biocontrol mechanisms since it is well-identified for 100% effectiveness in pest control. The mycelium of *T. viride* has shown its capabilities for the production of various types of enzymes, including cellulases and chitinase, with degradation capability for celluloses and chitin polymers, respectively. It is ubiquitous in nature. It is widely used for the management of crop diseases and is basically soil-borne, but it is also foliar. *Trichoderma* has shown its potential due to diversity, ecology, and application. The mechanism of action includes competition, production of different metabolites, induced resistance and enzymes, etc. There are several commercial formulations available all over the world that are used against crop diseases. *Trichoderma*, due to its potential for degradation capability, can be utilised from waste to wealth. Later on, with the development of more research on *Trichoderma*, various utilities were found. This includes its effective control against harmful insects in agricultural as well as health sectors. It also can detoxify the heavy metals. In the health sector, continuous exploration of its benefits for drug discovery is being done. As a whole, it can be considered soil gold and a promising future beneficial microbe.

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Introduction

There are several types of plant pathogenic microbes available on Earth. They are not only causing significant losses to the standing crops but are also responsible for post-harvest losses. There is an increase in demand for crop production due to the rise in the global population, and it is only possible to achieve via effective pest infection control for crop productivity (van Dijk et al. 2021). After getting knowledge of plant diseases, there needs to be a faster adoption of management practices. As a result, synthetic chemicals were used to manage plant diseases, and they have helped to increase crop production/ yield. However, knowingly or unknowingly, the use of synthetic chemicals as pesticides is found to intensify the effects of affecting the bird or human health and also other non-target biotic components in environments (Nicolopoulou et al. 2016). This has led scientists to start thinking of an alternative to chemicals, and biocontrol methods have been found to be one of the best options.

Biocontrol agents such as fungi, bacteria, and other beneficial microbes were widely used and commercialized for the management of several diseases

caused by pest/ insect infection, which affects crop productivity. Among the fungal biocontrol, the *Trichoderma* genus is found to be widely accepted and used for the management of plant diseases as an effective biocontrol agent (Naeimi et al. 2020). The genus *Trichoderma* is found under the division Ascomycota, class Sordariomycetes, and ordered Hypocreales as heierarchy details of this fungus. The reason for its wide acceptance as a biocontrol agent of *Trichoderma* is that it is ubiquitous and survives in all conditions of crop growth. At present, *Trichoderma* products are available in various forms, such as talc-based, liquid-based, and low-cost formulations. Species of *Trichoderma* are reported to be the best fungal organisms that exhibit the capability of pest/ insect infection control mechanisms. It can be utilized directly, and it exhibits parasitism and also produces secondary metabolites. There are other approaches of control mechanism by *Trichoderma* reported as the generation of antioxidant compounds and repellent metabolites (Poveda 2021). An indirect way of controlling pest infection in crops is reported via the activation of systematic plant defensive responses, and the attraction of natural enemies is discussed with other controlling mechanisms such as parasitism of insect-symbiotic microbial system. So, in current periods, *Trichoderma* is found to be an effective microbial agent against plant pathogens and insect pest control in crops, and it can be applied as a future alternative to control pests in crops. This fungal genus species utilization can help in the

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development of sustainable agricultural crop production with enhanced yield/ productivity with healthy food grain (Hewedy et al. 2020). Several research reports claim that it is a biocontrol agent for insect pest control, and it can be applied in direct and indirect ways as an effective biocontrol agent for pest control. Now, species of *Trichoderma* genus are widely studied and used as the best biocontrol agents in agriculture, and pathogenic fungi can exhibit this ability due to parasitizing the pest/ insect. Finally, they kill them as effective biocontrol agent by using the best pest control mechanisms compared to other approaches of pest control, such as physical or chemical or combinations of these two approaches (Poveda 2021; Sinha et al. 2023).

Fusarium oxysporum is a reported well-known soil-borne pathogen and it causes vascular wilt disease in many plants. For this control, the biocontrol mechanism can find the best option, and this approach of pest control can gain more importance in crop disease protection under a part of integrated approaches for managing pest/ fungal mediated diseases. In this context, different species of *Trichoderma* are applied as optimal candidates to control the *Fusarium oxysporum* infection (Diaz-Gutierrez et al. 2021). Reports have supported the effectiveness of *Trichoderma* mediated pest control in annual plants, and its efficacy is dependent on the application protocol/ formulations. Diaz-Gutierrez et al. (2021) have gone through the assessment for preventive/ curative potential of the rhizospheric *T. asperellum* UDEAGIEN-H01 strain, and it has worked against the *F. oxysporum* on the rooted cutting of *S. rebaudiana* (plant of Asteraceae family) (Chen et al. 2021). After thirty-three days of incubation, *F. oxysporum* infected stevia seedlings, which had up to 90% incidence, were found to have affected the disease. In contrast, only 10% of the *T. asperellum* pretreated plants and 70% of the post-treated stevia plants have shown *Fusarium* wilt symptoms. So, dual confrontation assays have proved the potential antagonistic effect of *T. asperellum* against *F. oxysporum* growth and infection capability (Sui et al. 2022; Singh et al. 2021). In another experiment, they claimed that applying a new strain, *T. asperellum*, exhibited the production capacity of phytohormones like salicylic and jasmonic acid. They have also explored other biocontrol mechanisms for pest infection, and these are found to be the secretion of cell-wall degrading enzymes like chitinase and cellulases (Li et al. 2020). The review discusses the species of the *Trichoderma* genus as the best biocontrol agent for pest infections in various crops, and it also discusses the control mechanism for pest infection due to the formulation of the *Trichoderma* genus as an alternative option to chemical pesticide for disease control.

1. Classification of *Trichoderma* species

1.1 Morphological-based identification

Originally, the first introduction of *Trichoderma* was done by Persoon (1794), and later, its sexual state was suggested as *Hypocrea* species (Tulasne & Tulasne 1865). Later on, in 1969, Rifai suggested four taxonomic equivalents based on characters such as growth, green conidia and conidiophore. He used the 'aggregate'

species for the identification of *Trichoderma* based on similar characters, which later became key identification characters for species identification. Using the 'species aggregates', *T. hamatum* was identified. The alternative of the *Trichoderma* was named *Pachybasium* (Bainier 1906), but most of the authors reject the concept. Bisset (1991), who has widely worked on the classification of *Trichoderma*, accepted the concept of *Pachybasium* under *Trichoderma*. He worked extensively on the morphological taxonomy and divided it into five sections, including *Trichoderma*. Due to great variation in morphology, most people do not have the experience required to identify *Trichoderma* species accurately. With the advancement of technology, the present classification system is mostly dependent on molecular tools for identification (Rodrigues et al. 2018).

1.2 Molecular characterization of *Trichoderma*

Due to problems and confusion over morphological studies on *Trichoderma* taxonomy, researchers focus on macromolecular-based identification of strains or species. It is to be observed that comparing the traditional one, nucleic-based or enzymatic characterization of the species is more accurate and has a greater impact. Nowadays, due to the rapid progress of detection methods, morphological methods have been replaced by modern biotechnological tools for identification. Identification at the species level was effectively performed by commonly used primers such as ITS 1, 2 and 4 and also by *tef1* gene. A barcode program of oligonucleotide-based TrichoKey v.1.0 and TrichoBLAST are widely accepted, and search tools are available at www.isth.info. International Subcommittee, which deals with the identification and characterization of *Trichoderma*, provides information on more than 200 species of fungus at its website: <http://www.isth.info/biodiversity/index.php>.

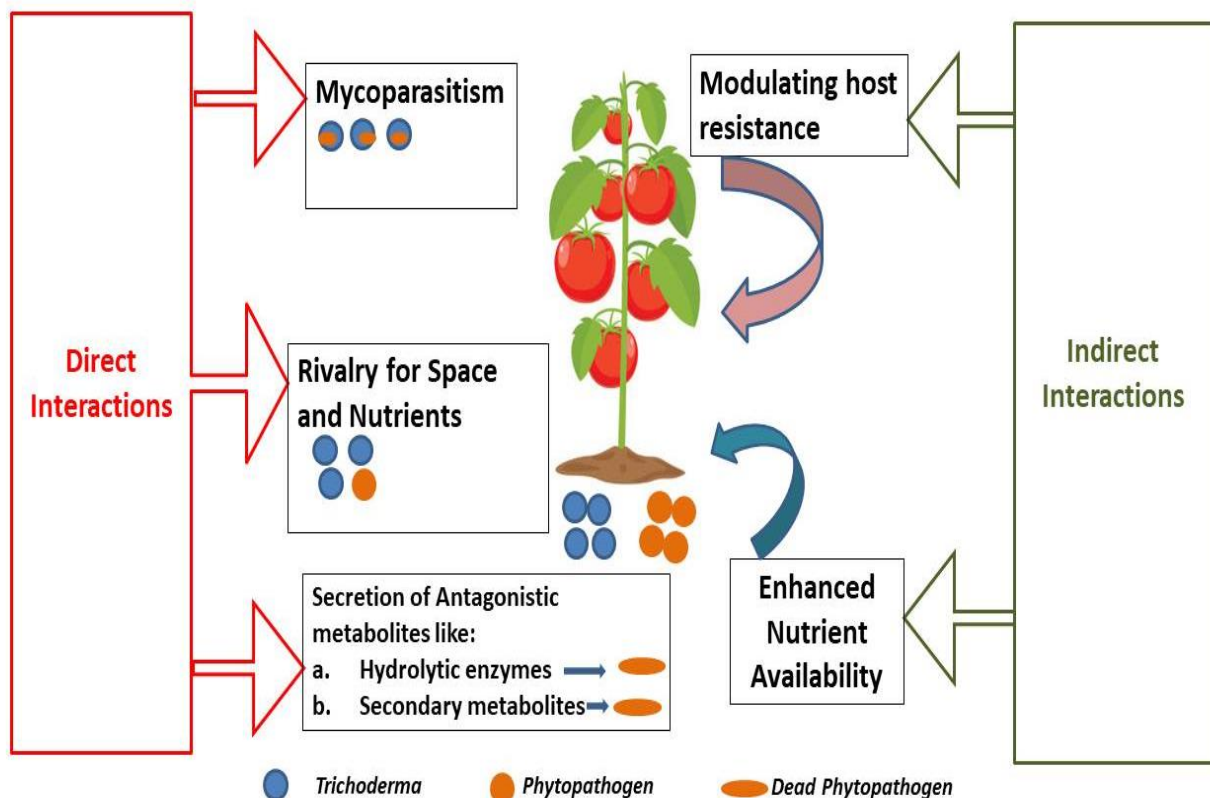
1.3 Mechanism of action

The mode of action for *Trichoderma* includes direct action of parasitism or indirect action, which provides for competition, antibiosis, induced resistance, and some act as endophytes. The myco-parasitism ability of *Trichoderma* is well studied by several workers against plant pathogens, and recent work on the role of AGL1 aegerolysin gene on functional characterization was studied on *Trichoderma atroviride* (Dubey et al. 2021; Haldhar et al. 2020). It competes with pathogens in several ways, including nutrition; among them root colonization is one of the critical factors. A gene-level study revealed the role of the expression of the *tvhdyii1* gene in increasing root colonization against the antagonistic activity of *R. solani* (Guzman-Guzman et al. 2017). Antibiosis is one of the biocontrol characteristics of *Trichoderma*. It produces several low molecular-weight chemicals which inhibit the pathogen's growth and sporulation. The involvement of the secondary metabolites and their effect on gene expression was studied in detail (Vinale & Sivasithamparam 2020). Several chemicals, such as salicylic acid, abscisic acid, jasmonic acid, etc., are essential for triggering induced resistance to plants. The plant produces such chemicals

(SA, JA, ET and ABA) triggered by *Trichoderma* application (Checker et al. 2018).

The role of *Trichoderma* as biocontrol is well understood. However, other than biocontrol activities, there are several benefits. With the advancement of research work, workers are tirelessly exploring the unexplored microbes in nature, and *Trichoderma*-related research is also one of them. These species are continuously exploring for the benefit of mankind. As a result, there is the finding of the plant growth promotion activities its beneficial effect on managing agricultural pests as well as pests related to

human diseases such as malaria vector, mosquitoes. In recent articles, some workers have studied the characterization of secondary metabolites for their use in agriculture, industrial, and drug discovery. Industrial application and drug discovery in relation to *Trichoderma* are gaining importance day by day as there is a wide range of biomolecules and findings from it. In view of its gaining importance, the present review is focused on the multipurpose roles of the *Trichoderma* for plant disease management, insect management as well as drug discovery and other useful purposes and applications.



Major mechanisms by which *Trichoderma* act as Biocontrol Agents

Figure 1. Direct and indirect interactions of *Trichoderma* as biocontrol agent

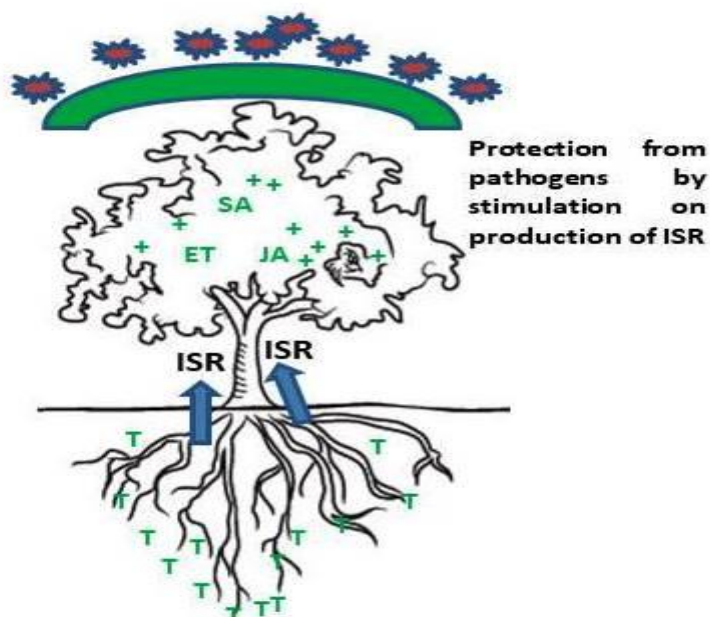


Figure 2. Induced Systemic Resistance (ISR) in plants triggered due to *Trichoderma* application (T-*Trichoderma*, JA- Jasmonic acid, SA- Salicylic acid, ET- Ethylene, + = Increase)

1.4 *Trichoderma*: Reservoir of bioactive molecules

The beneficial use of *Trichoderma* is well known as a biocontrol agent globally, is potentially due to the secondary metabolites that are chemically diverse in nature. The role of these metabolites in the management of plant diseases against plant pathogens has been widely reported. Other than direct disease management activities, these metabolites have diverse biological

activities like plant growth promotion, antibiotic, flavouring agents, weedicide properties, cholesterol regulating potential, anti-ageing, immune suppression, and antiparasitic capacities that cannot be overlooked. A list of major compounds isolated from *Trichoderma* with their potential application, as elaborated by Reino et al. (2008) is tabulated in Table 1.

Table 1. Class of major compounds with potential application reported and isolated from *Trichoderma* spp.

Class of Compound	Species	Potential Application	References
Antraquinones			
Coniothyronine	<i>Trichoderma harzianum</i>	Antifungal, antimicrobial activities	Shi et al. (2018)
Lentisone	<i>Trichoderma sp</i>	Antibacterial, antifungal activities	Qi et al. (2020)
Emodin	<i>Trichoderma harzianum</i>	Antimicrobial, Laxative, antiviral, antineoplastic activities and Cathartic	Qi et al. (2020)
Chrysophanol	<i>Trichoderma harzianum</i>	Anticancer, hepatoprotective, neuroprotective, anti-inflammatory, anti-ulcer, and antimicrobial activities	Yusuf et al. (2019)
Carotane Sesquiterpenes			
Trichocarotins (I – M)	<i>Trichoderma virens</i>	Antibacterial	Shi et al. (2021)
Methylhydroheptelidate	<i>Trichoderma virens</i>	Antibacterial	Song et al. (2020)
Pyrones			
Pyrone 6-pentyl-2H-pyran-2-one	<i>Trichoderma atroviride</i>	Flavouring agent (Coconut aroma), antibacterial, antifungal, modulation of plant defense mechanism	Lazazzara et al. (2021)
Viridepyronone	<i>Trichoderma viride</i>	Antifungal activity	Contreras-Cornejo et al. (2016)
Koninginin D	<i>Trichoderma koningii</i>	Antibiotic, antifungal activities	Lang et al. (2015)
Modified Dipeptides			
Trichodermamides A	<i>Trichoderma harzianum</i>	Cytotoxic, Antifungal activity	Harwoko et al. (2021)
Dithioaspergillazine A	<i>Trichoderma</i> sp. TPU199 (cf. <i>T. brevicompactum</i>)	Anticancer compound	Yamazaki et al. (2020)
Viridins	<i>Trichoderma virens</i> , <i>Trichoderma koningii</i> , <i>Trichoderma viride</i>	Antifungal activities	Sharma et al. (2020)
Viridiofungins	<i>Trichoderma viride</i>	Antimicrobial, antifungal, anticancer activities	Yan et al. (2021)
Nitrogenous heterocyclic compounds	<i>Trichoderma harzianum</i>	Antifungal activity	Contreras-Cornejo et al. (2016)
Azaphilones	<i>Trichoderma guizhouense</i>	Antioxidant activity	Pang et al. (2020)
Harzialactones	<i>Trichoderma harzianum</i>	Antileishmanial activity	Braun et al. (2021)
Butenolides	<i>Trichoderma</i> sp. FKI-5513	Anticancer	Fukuda et al. (2012)
Trichothecenes	<i>Trichoderma brevicompactum</i> , <i>T. albolutescens</i>	Antiviral, antifungal, antimicroalgal activity	Shi et al. (2020)
Isocyano metabolites	<i>Trichoderma hamatum</i>	Antibiotic activity	Ma et al. (2021)
Diketopiperazines	<i>Trichoderma virens</i>	Antifungal activity	Kim et al. (2019)
Peptaibols	<i>Trichoderma virens</i>	Anticancer activity	Casagrande et al. (2021)

1.5 Biological activity of biomolecules from *Trichoderma*

The diverse biomolecules found in different species/strains of *Trichoderma* are excellent reservoirs of potentially beneficial biological activity that can be exploited for drug discovery. These molecules have been studied in different models of experiments, like cell lines to animal diseases and are sustained with data obtained from different *in vivo* models (Zhang et al. 2021). The lucrative potential of *Trichoderma* as an efficient biocontrol agent is potentially due to its ability to secrete diverse secondary metabolites (Zellinger et al. 2016). Historically, fungi have been a source of a vital source of drug discovery, with the most pathbreaking flora, such *Penicillium*, providing the first antibiotic to mankind. Since the discovery of penicillin, the chemical exploration of fungal secondary metabolites has been undertaken with keen enthusiasm. Zhang et al. (2021) reported a total of 203 compounds from *Trichoderma* from literature published from 2009 to 2020. Biocontrol agents impact the host plants by modulating the biological system of hosts through a diversity of metabolites secreted by them (Druzhinina et al. 2011). The mode of action of *Trichoderma* is also too similar to the way probiotics modulate their benefit in animal models. The gene expression of the gut microbiome of bacterial transcripts is over 3 million, and these gene products play an

important role in immune response and metabolism (Braundmeier et al. 2015). Similarly, studies revealed that thousands of genes of *Trichoderma* influence the host plant through reprogramming by an adaptive array of several transcriptomes of *Trichoderma* in relation to hosts (Sharma et al. 2017).

2. *Trichoderma* as crop friendly microbe

2.1 Soil-borne plant diseases and *Trichoderma* activity

In general, the production of crops is hampered by various biotic and abiotic factors such as pests and diseases (biotic) and environmental factors (abiotic). Among the biotic factors, diseases caused by soil-borne microorganisms are difficult to manage. Management of soil-borne diseases by soil drenching is not only economically viable but also harmful to the environment (Ferreira et al. 2021). So, here comes the use of biocontrol agents, among which *Trichoderma* is one of the best and most widely used (Abdullah et al. 2021). There is the availability of more than 77 commercial formulations of *Trichoderma* which contributes 50-60% of the total BCAs all over the world. Among the commonly used strains are *Trichoderma viride*, *T. harzianum*, *T. asperellum*, *T. virens* etc. (Fanelli et al. 2018). Some selected examples of the literature cited for the management of soil-borne plant pathogens by *Trichoderma* are illustrated in Table 2 and Figure 2.

Table 2. List of some *Trichoderma* used against soil-borne pathogens

Crops	Pathogen	Biocontrol Agent	References
Cereals			
Rice	<i>Rhizoctonia oryzae-sativae</i>	<i>Trichoderma</i> spp	Vignesh et al. 2019
Rice	<i>R. solani</i>	<i>Trichoderma</i> spp	Chakrapani et al. 2019
Maize	<i>Cephalosporium maydis</i>	<i>Trichoderma</i> spp	Elshahawy et al. 2018
Vegetables			
Tomato	<i>Fusarium</i>	<i>T asperellum</i>	Li et al. 2018
Potato	<i>Streptomyces</i> spp	<i>Trichoderma</i>	Zhenshuo et al. 2019
Chilli	<i>Fusarium</i> sp	<i>Trichoderma</i> sp	Trina et al. 2017
Ghost pepper	<i>Rhizoctonia solani</i>	<i>Trichoderma</i> spp.	Khedarani & Bireswar 2018
Cucumber	<i>Fusarium</i>	<i>Trichoderma</i>	Chen et al. 2018
French bean	<i>Sclerotium rolfsii</i> Sacc	<i>Trichoderma</i> sp	Rajlakshmi & Sinha 2014
Fruits			
Papaya	<i>Fusarium solani</i>	<i>Trichoderma</i> spp	Izquierdo Garcia et al. 2020
Apple	<i>Fusarium</i> species	<i>Trichoderma</i> spp	Wang et al. 2022
Citrus	<i>Phytophthora</i> spp	<i>Trichoderma</i> spp	Choudhary et al. 2021
Grapes	Powdery mildew	<i>Trichoderma</i> spp	Pascale et al. 2017
Gooseberry	<i>Fusarium</i> wilt	<i>T. virens</i>	Izquierdo Garcia et al. 2020
Other crops			
Mustard	<i>R. solani</i>	<i>Trichoderma</i> sp	Nirupama et al. 2017
Chickpea	<i>Fusarium</i> sp	<i>Trichoderma</i> sp	Tampakleima et al. 2017
Groundnut	<i>Sclerotiumrolfsii</i> Sacc	<i>Trichoderma</i> sp	Rashmi et al. 2017

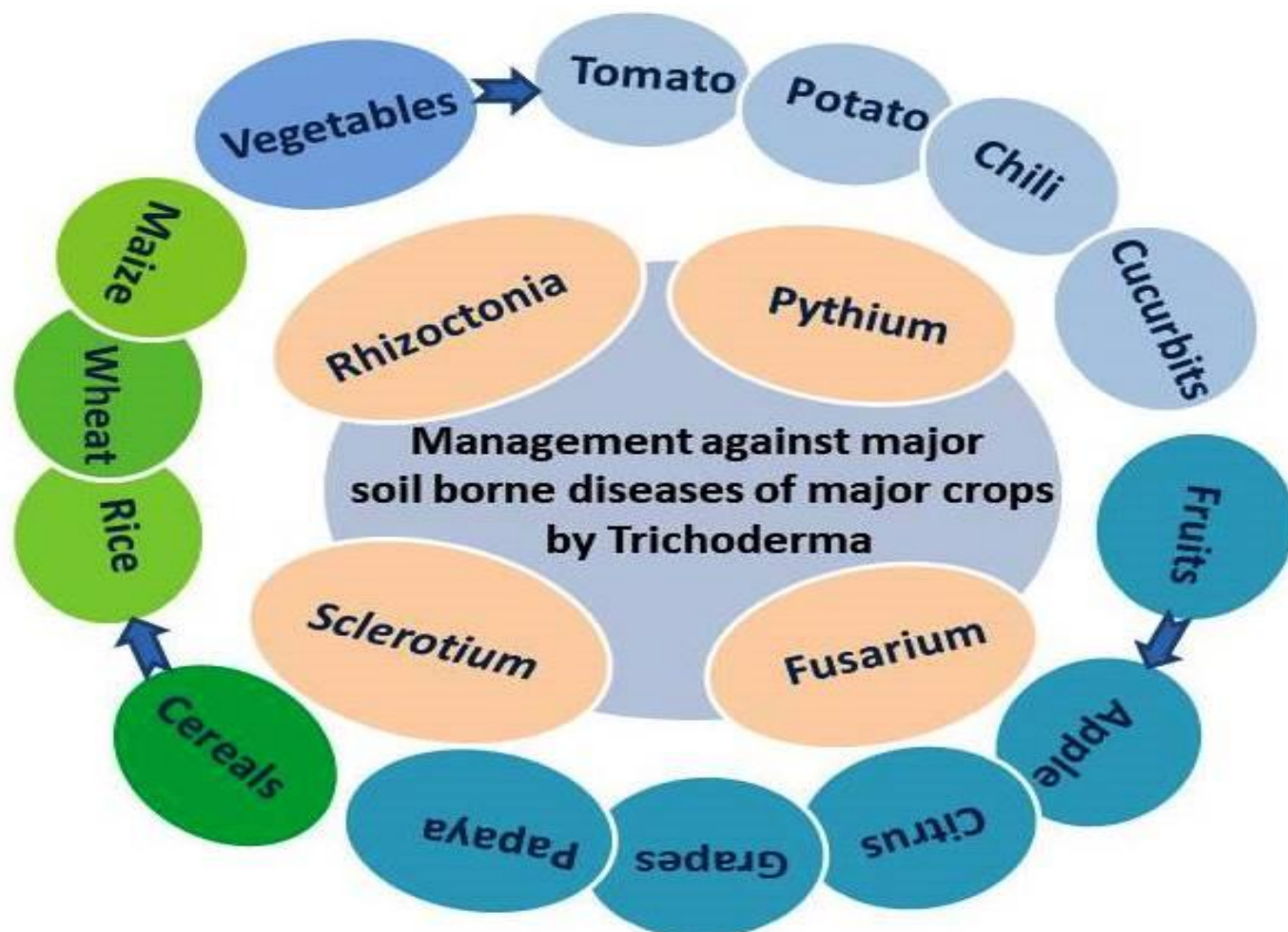


Figure 3. *Trichoderma* for management of soil-borne diseases of crops

2.2 Foliar plant diseases and *Trichoderma* action

The phyllosphere and the fructosphere are unprotected from the harsh gaseous atmosphere and face sharp fluctuations in temperature and surface wetness, vapour water pressure deficit, gases, air pollutants, wind, radiation, etc., in contrast to the rhizosphere, which is buffered in the biological, chemical, and physical soil environment. As a result, the foliar environment differs significantly from the soil environment, and the epiphytic microbial populations significantly diverge from the populations in the rhizosphere. Bacteria, filamentous fungi, actinomycetes, protozoa, and algae are just a few of the varied microfloral species that can grow and function in the rhizosphere. These populations are constantly evolving as a result of changes in the phyllosphere's physical, chemical, and nutritional environments. As a result, the phyllosphere is regarded as a challenging environment for biological control since the used biocontrol agent must be able to establish, grow, and maintain its antagonistic potential in the more challenging and frequently changing foliar environment.

2.3 *Botrytis* blight or gray mold disease and *Trichoderma* action

Botrytis cinerea is a ubiquitous, necrotrophic fungus that causes grey mould. It preys on the leaves, flowers, and fruits of numerous field and greenhouse-grown crops, including grapes, strawberries, tomatoes, cucumbers, beans, onions, roses, gerberas, begonias, carnations, chrysanthemums, marigolds, petunias, and others. It also

causes post-harvest losses to important vegetables (tomato, pepper, eggplant) and fruits (grape, pear, cherry, etc.) (Elad et al. 2016). In most cases, microbial bioagents, like fungi, bacteria, and yeast, can effectively reduce losses by antibiosis (Kasfi et al. 2018), competition and secondary metabolites (Mulero-Aparicio et al. 2019), parasitism (Khol et al. 2019), and initiation of plant defense (Mhlongo 2018). *Trichoderma* is efficient for managing soil-borne and foliar diseases. One of the successful *Trichoderma* species and isolates being tested for foliar disease management is *T. harzianum* Rifai strain T39, which was initially chosen and made available for the treatment of *Botrytis* diseases (Yadidia et al. 2003). The *T. harzianum* T39 formulation's effectiveness in combating grapevine grey mould disease was the subject of arguably the most thorough evaluation. Similar to this, *T. harzianum* T39 (Trichodex) at 0.2 g per l was also capable of successfully eradicating grey mould in greenhouse-grown tomato and cucumber plants (Marra et al. 2006). Additionally, *Trichoderma* has been used to manage *Botrytis cinerea* on strawberries biologically (Harman et al. 2004). The grey mould disease on snap bean was lessened by the inhibitory volatile chemicals produced by *Trichoderma hamatum*, *T. harzianum* T39 (Elad 2000).

2.4 Powdery mildews and *Trichoderma* action

Powdery mildew is caused by Erysiphales, an obligate parasite. It is one of the most economically important foliar disease of crop plant (Babosha et al. 2020).

Because of the bio-agent's inhibitory effects, competition for space and food sources, and production of antagonistic chemicals, *Trichoderma* spp. also suppresses the powdery mildew illness. Seed treatment with *Trichoderma* induced resistance against powdery mildew and significantly enhanced plant growth (Sawant et al. 2017). *E. heraclei* treated with *Trichoderma* spp. reduced percentage of conidia germination, and length of germ tube under *in vitro* studies (Ahmed et al. 2021). *Trichoderma* produces several enzymes such as endochitinase, chitobiosidase, n-acetyl-glucosaminidase, and glucan 1, 3-glucosidase, which severely inhibits spore germination and germ tube lengthening (Abo-Elyousr et al. 2020). The findings of Amin et al. (2018) revealed that *Pseudomonas fluorescence* and *Trichoderma viridi* (both at 75% concentration) were shown to be much more effective biocontrol agents than *T. virens* in treating powdery mildew and black spot diseases of roses in field settings. *Pseudomonas fluorescence* and *Trichoderma harzianum* produce antifungal compounds, including gliotoxin and certain growth regulators, which help to inhibit disease. These substances are amphiphilic membrane active surfactants that, when applied to plant surfaces, enhance plant resistance. These forces treated plants to create metabolites that inhibit pathogen growth as well as growth promoters like indols that boost plant growth in general. This decrease may be attributable to the evaluated bio-agent potential as PGPR, which is frequently used to control plant diseases (Prasad et al. 2017). Using *T. harzianum* and *T. viride*, Hafez et al. (2018) reported that controlling *P. xanthii* caused powdery mildew in cucumbers by about 40% (Zhang et al. 2018).

2.5 Downy mildew and *Trichoderma* action

Trichoderma atroviride TRS25 revealed control ability against cucumber downy mildew. After the application of TRS25, the activities of plant defence enzymes such as guaiacol peroxidase, ascorbate peroxidase, and phenylalanine ammonia-lyase were elevated in cucumber leaves (Szczec et al. 2017). According to Prasetyo et al. (2019), *Trichoderma* spp. treatments might lessen the development of downy mildew in maize at 4 and 5 days after inoculation. Still, they were unable to reduce the severity of the disease or increase the plant's stover dry weight.

2.6 Anthracnose and *Trichoderma* action

Anthracnose is considered one of the essential foliar and post-harvest diseases of crops. It is caused by *Colletotrichum* spp. having an adverse effect on the cultivation and production of common crops such as mangoes (Li et al. 2020), tomatoes (Diao Z et al. 2014), and chili peppers (Oo & Oo 2019). In PDA-assayed plates, *T. koningiopsis* PSU3-2 outgrew *C. gloeosporioides* and effectively inhibited its growth, suggesting a competition mechanism involved in biocontrol activity (Ruangwong et al. 2021). According to Devamma et al. (2021), *Trichoderma harzianum* (Madanapalle field isolate) showed the most significant inhibition of *Colletotrichum gloeosporioides* mycelial growth (73.50%), which was followed by *Trichoderma viride* (Palamaner field isolate) (60.43%). *Trichoderma harzianum* (Punganur field isolate)

(29.70%) showed the slightest inhibition. Effective management of the mango anthracnose disease, minimum 3 spraying on leaves and fruits by *T. harzianum* showed a better reduction of the disease incidence (Sharma et al. 2021).

3. *Trichoderma* for efficient and environment-friendly insect/pest management

Trichoderma is one of the essential genera of fungi that reside in rhizosphere soil. Its efficacy has been reported by several workers from various parts of the world with diverse geographical areas. The genus is characterized by variations in morphology and colony pigmentation. The colour of the colony may vary from green, yellow, yellow, green and white. The tufts of conidiophores have a distinctive branching pattern along with the presence of short sterile phialides on which conidia are formed (Mukhopadhyay & Kumar 2020). The shape of the conidia varies from globular to sub-globular, ellipsoidal, sub-ellipsoidal, ovoid, and sub-cylindrical. *Trichoderma* produces single-celled and thick-walled chlamydospores either in the intercalary or terminal manner. This genus is mainly recognized as a potential biocontrol agent of several forest and agricultural plants. It has also been successfully utilized to manage several agricultural pests (Poveda 2021). Several *Trichoderma* species not only efficiently managed several soil-borne plant pathogens but also served as a promising biofertilizers, thereby enhancing crop production. This fungal genus is also known for its notable role in the bioremediation of soil, as the fungi release several enzymes which degrade polycyclic aromatic hydrocarbons and heavy metals. *Trichoderma* species are enzymatically active and produce several enzymes, namely, cellulase, hemicellulase, chitinase, proteases, lignin-degrading enzymes, glycoside hydrolases, polygalacturonase and β -1,3glucanase. It produces several metabolites, including terpenes, pyrones, gliotoxins, polyketides, peptaibols, trichothecene, harzianopyridone, viridofungin, trichotoxins, trichoderminol, trichodermin, trichoderic acid, harzianic acid, etcetera (Al-Ani 2019). These fungi also released several volatile compounds, including sesquiterpenes, aldehydes, ketones, alcohols, esters, alkenes, amines, thiols, monoterpenes, etcetera. These enzymes and metabolites are effective against several insect pests and phytopathogens.

Urban insect pests annoy humans, animals and plants. This group of pests resides in residential buildings and other man-made engineered structures. They inflict irritation, spread diseases and affect the economic and aesthetic value of life. Mosquitoes not only bite and irritate but also act as carriers of several diseases. Other remarkable urban insect pest includes cockroach, ant, bed bug, houseflies, fruit fly, termites, etcetera. *Trichoderma* can be utilized to manage insect pests successfully. *Trichoderma* affects insects either directly or indirectly through the employment of various mechanisms. The exploitation of *Trichoderma* for managing urban pests is one of the significant management strategies as it is environmentally friendly and leaves no harmful residue. Hence, a thorough understanding of the insecticidal mechanisms employed by *Trichoderma* in the management of urban pests,

including blood-feeding insects, household insects, destructive eusocial insects and future prospects of *Trichoderma* in the management of urban insect pests are considered very essential.

3.1 Mechanism of insect's management by *Trichoderma*

Trichoderma is one of the potential bio-control agents for managing insect pests. It exerts detrimental impacts on several insects through the employment of diverse mechanisms. This genus directly attacks the insect itself or its symbiont partner. It also employs indirect mechanisms through the release of secondary metabolites, which in turn confers repellence and feeding deterrence to a particular insect. This group of fungi releases volatile compounds which induce mortality and also reduce the rate of reproduction in insects through the interruption of ergosterol production, which is coupled with the accumulation of squalene (Alvarez-Garcia et al. 2022). It has detrimental impacts on different developmental stages of insects, thereby delaying the emergence of the adult stage. Metabolite produced by *Trichoderma* confers changes in the feeding activities of insects due to deterrence impacts (Ratnaweera et al. 2021). The chitinase enzyme produced by *Trichoderma* affects the peritrophic matrix of the insect midgut. The permeability of the midgut was altered due to the splitting of superficial layers and the disintegration of fibril networks of the peritrophic matrix, which in turn interfered with the development and growth of the larvae. Secondary metabolites produced by *Trichoderma* also exert repellence activity on certain insects (Rodriguez-Gonzalez et al. 2020). *Trichoderma* species parasitizes insects and grow on the insect bodies, causing severe mycosis, which is often associated with the mycelial growth of *Trichoderma* on the surface of the insect's body (Ghosh et al. 2021). Its spore causes blockage of spiracles in cockroach as a result of spores germination on the insect's body, leading to obstruction of small spiracle openings, which subsequently affects the respiratory system in cockroach. Similarly, spraying of *T. asperellum* suspension on larvae of *Anopheles* species resulted in the death of the larvae through mechanical obstruction of spiracles and mouth by fungal spores. Several enzymes produced by *Trichoderma* are associated with parasitism in insects. Chitinolytic enzymes of *T. asperellum* cause the degradation of cuticle in third instar larvae of *A. aegypti* (Silveira et al. 2021). All three layers of the cuticle, namely, epicuticle, exocuticle and endocuticle, were ruptured. The thorax and head of the third instar larvae were ruptured, which is accompanied by deterioration of the exoskeleton into a shapeless mass. Degradation of larval cuticle facilitates the adsorption of antibiotics. When *Trichoderma* is exposed or fed directly to insects, it causes autolysis and desiccation (Stefanelli et al. 2020). *T. asperellum* affects phenoloxidase activity thereby decreasing phenol oxidase content in the hemolymph and cuticle of mosquito larvae. Ghosh et al. (2021) outlined the bio-larvicidal mechanisms of *T. asperellum* TaspSKGN2 against *Anopheles* mosquitoes. Mucilage secreted by the fungus aids in the attachment of *Trichoderma* conidia to

the mosquito larvae. The spore then germinates and subsequently releases cuticle-degrading enzymes, namely, chitinase, proteases and spore-bound Pr1. The spore then penetrates the cuticle with an infected peg and enters the larval body. The hyphal of the fungus grows and proliferates, followed by active sporulation. The fungus secretes toxin, which interacts with larval hemocytes. It is preceded by a subsequent decrease in the level of phenol oxidase followed by degeneration of hemocyte cells through nuclear fragmentation and nuclear deformities. The mosquito larvae immunity system is completely broken down. The larval alimentary system becomes smaller and deformed. This is preceded by the death of mosquito larvae. The spore produced inside the dead larvae germinates. The hyphae of the fungus start growing and proliferating outside the larvae cuticle. Silveira et al. (2021) professed that the enzymatic activity of β -1,3-glucanase, N-acetylglucosaminidase and chitinase of *T. asperellum* disintegrates cuticle in L3 larvae of *A. aegypti* coupled with deterioration of larval exoskeleton. *Trichoderma* also efficiently managed insects indirectly by attacking the symbiont partner of the insects. The symbiont partner of leaf-cutting ant namely, *Attamyces* and *Luecoagaricus* species, are parasitized by *Trichoderma*.

3.2 Management of blood-feeding insects

Mosquitoes are a nuisance to humans and animals. Mosquitoes bite causes irritation, swelling, itchiness and redness. They are also vectors of several diseases. *Aedes aegypti* is a carrier of arboviruses, including zika, chikungunya, yellow fever and dengue (Powell 2018). *Anopheles* species is a vector of malaria. *Trichoderma* can be employed for the management of mosquitoes as well as the spread of several diseases vectorised by mosquitoes. *T. viridis* is a promising oviposition attractant that can be utilized as bait for trapping female adults. *Culex quinquefasciatus* is used to manage mosquito populations substantially. The utilization of nanotechnology in the application of *Trichoderma* against mosquitoes is one of the efficacious approaches to managing several mosquito-borne diseases. Mycosynthesized silver nanoparticles of *T. harzianum* extracellular filtrates are efficient against the developmental stages of *A. aegypti*. Podder & Ghosh (2019) deliberated on the bio-efficacy of *T. asperellum* TaspSKGN2 for managing *Anopheles* species. Application of fungal spore suspension resulted in the death of the mosquito due to blockage of the spiracle and mouth of larvae by the fungal conidia. Administration of methanolic extraction of *T. asperellum* TaspSKGN2 leads to a reduction in phenoloxidase activity in the hemolymph and cuticle of *Anopheles* larvae. A study on the mass spectrometry analysis of *T. asperellum* filtrates confirmed the presence of insecticidal compounds, namely 2,3-di hydro thiopene, dihydro-6-methyl-4H-Pyran-4-one, alpha-pinene, 8-methyl quinoline, p-cymene, methyl ester and hexadecanoic acid. Silveira et al. (2021) described the bio-larvicidal efficiency of *Trichoderma* against *A. aegypti*. The chitinolytic enzymes of *T. asperellum* were identified and assessed against mosquito larvae. The enzymatic complex comprising

chitinase, N-acetylglucosaminidase and β -1,3-glucanase show prominent larvicidal activity, leading to impairment of molting of third instar larvae to fourth instar, which successively led to considerable mortality of the mosquito larvae. de Olivera et al. (2021) stated the bio-larvicidal potential of *T. atroviride* 1133 against *A. aegypti*. Ghosh et al. (2021) studied the bio larvicidal mechanisms of *T. asperellum* TaspSKGN2 against *Anopheles* species. Application of methalonic extracts of *T. asperellum* resulted in mortality of the mosquito larvae and complete loss of larval immunity system due to nuclear fragmentation of hemocyte cells.

3.3 Management of household insects

Trichoderma species have an insecticidal effect on cockroach. Abdul-Wahid & Elbanna (2012) delineated the usage of *T. harzianum* in managing American cockroach (*Periplaneta americana*). The exploitation of the fungal spore suspension, either as food additives or spray, was effective in managing the American cockroach. They observed the blockage of cockroach spiracles by fungal spores, which led to the subsequent death of the insect. Application of *T. harzianum* mycelialmat on the cockroach resulted in autolysis due to secretion of chitinolytic enzymes. The mortality of third instar larvae of houseflies increases with increased spore concentration of *Trichoderma*. Comparably, Al-Olayan (2013) disclosed the potential of *T. viride* against the larval and adult stages of housefly. Two *Trichoderma* species namely, *T. longibrachiatum* and *T. harzianum* efficiently managed the mediterranean fruit fly (*Ceratitis capitata*) resulting in a reduction of survivability of adult and fecundity of female along with an increase in male sterility. Atriztan-Hernandez et al. (2019) detailed the secondary metabolites production of *T. atroviride* in response to the feeding of *Trichoderma* by third instar larvae of *Drosophila melanogaster*. Consumption of *T. atroviride* mutant Δ tmk3 hindered the larval development and resulted in the death of the larvae. *T. atroviride* produced metabolite C₈ compounds, which are feeding deterrents of the fungus itself and also exert neurotoxic impacts that hinder the development of larvae.

3.4 Management of destructive eusocial insects

Odontotermes formosanus is a fungus, cultivating on termite which is well known for tunnelling and building a nest under the ground soil. This species of termite posed a threat to the man build structures, including dams and dykes. This termite harbours the agaric fungus *Termitomyces*, the fungus comb. This mushroom, in turn, serves as food for the termite population, thereby maintaining a symbiotic relationship. Some species of *Trichoderma* are competent bio-control agents of this

subterranean termite. Treatment of soil with *Trichoderma* affects the tunnelling activities of *O. formosanus*. Some *Trichoderma* species repelled the termite workers. In the soil treated with *Trichoderma* spp, the termite workers produced a few tunnels. Similarly, food substrate treated with *Trichoderma* sp. repelled another fungus-growing termite *Macrotermes natalensis*. *Coptotermes*, an important genus of subterranean termite attacks on living trees as well as on woods in residential housing areas (Kalleshwaraswamy 2022). *Trichoderma* strain FHG003 was isolated from the infected mycobiome of *C. testaceus*. The strain FHG003 produces pentapeptide FE011 and another cluster of metabolites which may be involved in the shifting of the microbiome of *C. testaceus* in relation to fungal infection. Leaf-cutting ants are a nuisance in urban areas. Montoya-Lerma et al. (2012) stated that apart from being an agricultural and forest pest, they are involved in the defoliation of vegetables and fruits in kitchen garden, ornamental plants in parks, gardens, living fences, streets and other green areas of the urban sites. Moreover, nesting leaf cutter ants on creeks in river banks, buildings, and soil damaged civil engineered structures holding the river bank, damaged the buildings themselves, and conferred instability of soil due to alteration of chemical and physical properties, respectively. *Atta cephalotes* a genus of leaf-cutting ants grows as symbiotic fungal partners on which they later feed. Lopez & Orduz (2003) demonstrated the effectiveness of *T. viride* against *A. cephalotes*. The application of *T. viride* by baiting techniques leads to mortality for both the ant population and its symbiont partner. The white veil of *T. viride* was observed covering *Attamyces* species. *T. lignorum*, in combination with *Beauverria bassiana* was competent in managing *A. cephalotes* as both the fungus targets the ant and its symbiont partner *Leucoagaricus gongylophorus*. Spraying of spore suspension of *T. harzianum* causes the death of *A. sexdansi* colony and also imparts deleterious effects on the fungal symbiont partner. Steffanelli et al. (2021) deliberated on the potential of *T. harzianum* in managing *A. sexdansi* *rubropilosa*. *T. harzianum* causes mortality of larvae, pupae and adult stages. However, it exhibited greater pathogenicity in larval and pupal stages. In another study conducted by Steffanelli et al. (2021), varying numbers of *Trichoderma* contaminated worker ants and healthy worker ants were intermixed and cultured in a colony. It was observed that the survival rates of the ant colonies became lower with increased incorporation of *Trichoderma* contaminated worker ants with the healthy worker ants.

Table 3. Management of insect pests of urban importance by *Trichoderma* species

<i>Trichoderma</i> specie	Insect pest	Mode of application of <i>Trichoderma</i>	Significant remarks	Reference
<i>T. viride</i> T26	<i>Atta cephalotes</i>	Baiting	Attack on symbiont partner	Lopez & Orduz 2003
<i>T. harzianum</i>	<i>Periplaneta americana</i>	Feeding and spraying of fungal spore suspension	Blockage of spiracles and autolysis in cockroach	Abdul-Wahid & Ebanna 2012
<i>T. harzianum</i>	<i>Aedes aegypti</i>	Exposure of mosquito larvae and pupae of extracellular <i>Trichoderma</i>	Exhibited vigorous larvicidal and pupicidal activity	Sundaravadivelan et al. 2013

		filtrates		
<i>T. atroviride</i>	<i>Drosophila melanogaster</i>	Feeding	Larval death and delayed larvae into adult flies	Artiztan-Hernandez et al. 2019
<i>T. lignorum</i>	<i>A. cephalotes</i>	Direct application of fungal spore suspension	More effectively used with <i>Beauveria bassiana</i>	Daza et al. 2019
<i>T. asperellum</i> TaspSKGN2	<i>Anopheles</i> species	Released larvae into a beaker containing fungal spore	Methanolic fraction 8 of <i>T. asperellum</i> expressed the most muscular larvicidal action.	Podder & Ghosh 2019
<i>Trichoderma</i> spp	<i>Odontotermes formosanus</i>	Soil treatment	Lower aggregation and tunnelling activities of the termites.	Xiong et al. 2019
<i>T. asperellum</i> TaspSKGN2	<i>Anopheles</i> species	Released of third instar larvae into fungal spore	Leads to nuclear deformities and nuclear fragmentation of hemocytes.	Ghosh et al. 2021
<i>T. harzianum</i>	<i>A. sexdans</i>	Baiting and spraying of fungal spore suspension	Leaf-cutting activity was significantly reduced	Filho et al. 2021
<i>T. asperellum</i> ENZT00	<i>A. aegypti</i>	Released of third instar larvae into a flask containing chitinolytic enzymes derived from <i>T. asperellum</i>	Fungal chitinolytic enzymes deteriorate the cuticle of mosquito larvae	Silveira et al. 2021
<i>T. harzianum</i>	<i>A. sexdans rubropilosa</i>	Individuals were dipped in <i>Trichoderma</i> spore suspension	Intense larvicidal and pupicidal action were observed in the first case.	Stefanelli et al. 2021

3.5 Prospects of *Trichoderma* in the management of urban insect pests

Trichoderma are potential biopesticides for managing a diverse group of insect pests. This fungal species can be utilized as an attractant for baiting or trapping certain insects. *T. longibrachiatum* and *T. hamatum* significantly attract fungi-growing termites *Odontotermes formosanus*. The formulation of *T. viride* also serves as an ovipositional attractant for female mosquitoes *C. quinquefasciatus*. This attractant potential of *Trichoderma* can be utilized in the baiting or trapping approach of pest management. Mycosynthesized nanoparticles of *Trichoderma* species are reported to exhibit insecticidal activity. The exploitation of nanotechnology to develop myco-synthesized *Trichoderma* nanoparticles provides an effective yet environmentally friendly approach to combating unwanted insect pests. The combination of *Trichoderma* with other entomopathogenic fungi and bacteria increases the insecticidal activity and confers more deleterious effects on the insect pests (Nawaz et al. 2020). *Trichoderma* can parasitize the insect symbiont partner, thereby annihilating the insect's food source. Other prominent mechanisms of *Trichoderma* against insects include parasitism, antibiosis, deterrent and repellent activities. Hence, *Trichoderma* species have a tremendous bio-potential against insects and can be employed either alone or utilized in integrated pest management strategies.

4. Role of *Trichoderma* as environment waste management (heavy metal cleaner)

The challenging task that's put forth by advancing the world is polluting nature, both soil and water with

xenobiotic chemicals. Xenobiotic compounds are newly introduced chemicals to the existing biological system, in addition to the naturally occurring minerals compounds in nature. Different categorized xenobiotics hold hydrocarbons, pesticides, poly aromatic hydrocarbons, polychlorinated aromatics, solvents, and other materials, including plastics, silicones, and surfactants. These chemicals get discarded after their use, and lodged xenobiotics exert harm to nature by interacting with the natural cycles. To immaculate the xenobiotic-contaminated soils and water, various techniques are enforced, which might be physical, chemical or biological techniques considering the properties of the pollutant and the one being polluted (Mule & Melis 2000). Adopting the conventional physio-chemical methods to remediate the polluted agents poses both advantages and disadvantages. Taking into consideration disadvantages, additional byproducts which are toxic to living are added. The comparative studies let out that bioremediation can be implanted for the best results from other techniques which is also a low-cost alternative. These bioremediation methods either stabilize or dispose-off the pollutants without disintegrating the organic compounds. Microorganisms can be employed everywhere and are a major part of the universe, which drives dynamic responsibilities to maintain stature and nature by scavenging pollutants. Among which *Trichoderma* spp. an extraordinary fungus possesses this nature of remediation, besides its multifaceted functions of being antagonistic to pests and pathogens, properties of PGPR and resistance to various agrochemicals and they also resistant to a wide good extent of toxicants viz., organometallic compounds, heavy metals, tannery

emissions and harmful compounds including cyanide (Ezzi & Lynch 2005). These multifaceted properties of this fungal genus widen the chances of its exploration as

a genetic resource that can be employed in making the environment pristine.

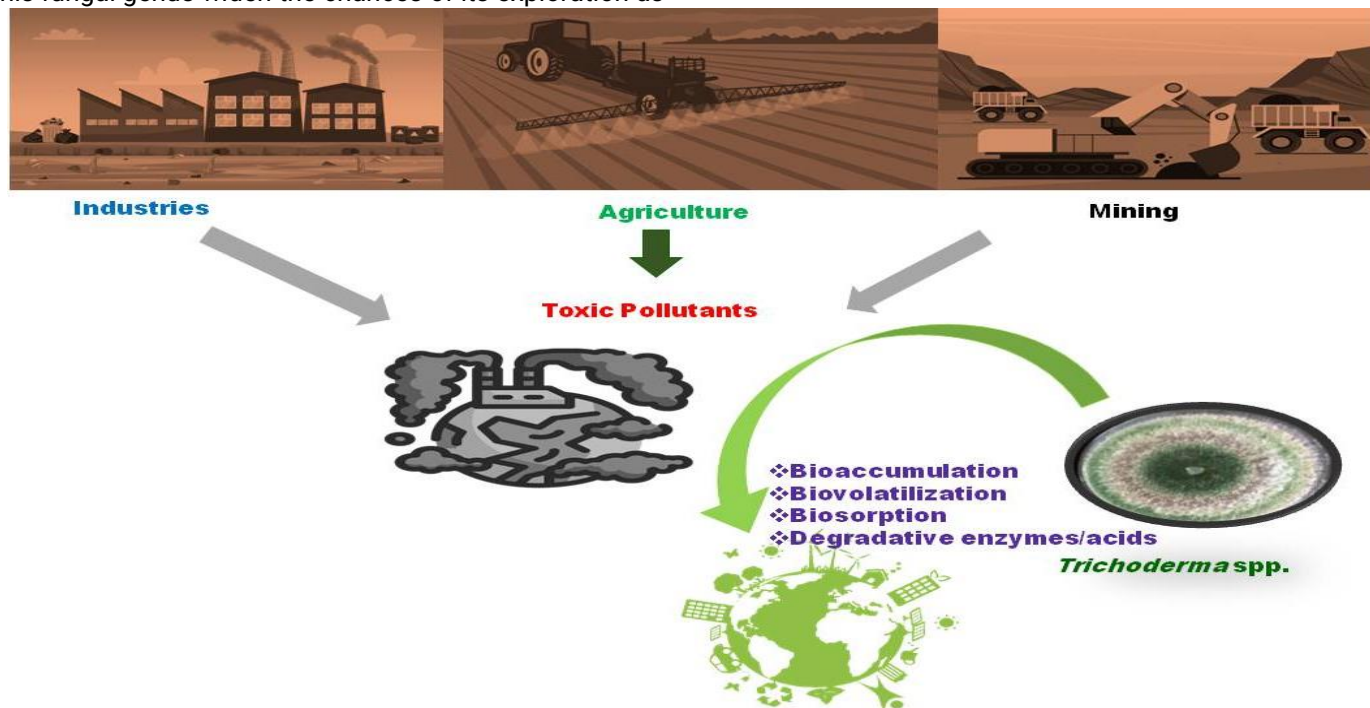


Figure 4. Heavy metal degradation by *Trichoderma*

4.1 Bioaccumulation

This technique involves the involvement of actively living cells for the deletion of metal that employs a dependent influx energy mechanism. Till date, several spp. of *Trichoderma* has deliberately exposed their nature to withstand and accumulate many heavy metals, namely arsenic, cadmium, copper, and zinc, under aseptic conditions (Zeng et al. 2010).

4.2 Biovolatilization

The transformation of compounds of metals (organic and inorganic) and metalloids to volatile derivatives by the action of enzymes through intercellular biochemical reaction is biovolatilization or biomethylation. The biovolatilization process for arsenic removal from liquid

media was done by using *T. asperellum* and *T. viridae* (Srivastava et al. 2011).

4.3 Biosorption

It's the ability of the biological agents that can accumulate pollutants and heavy metals from waste water by engulfing them metabolically or by the physico-chemical up taking action. The reaction proceeds when the negatively charged free groups bind metabolism independently to several bio-polymers, which results in the formation of the cell wall of the microbes. Biosorption for heavy metals is an alternative method for freeing water that is polluted with heavy metals (Ayad et al. 2018).

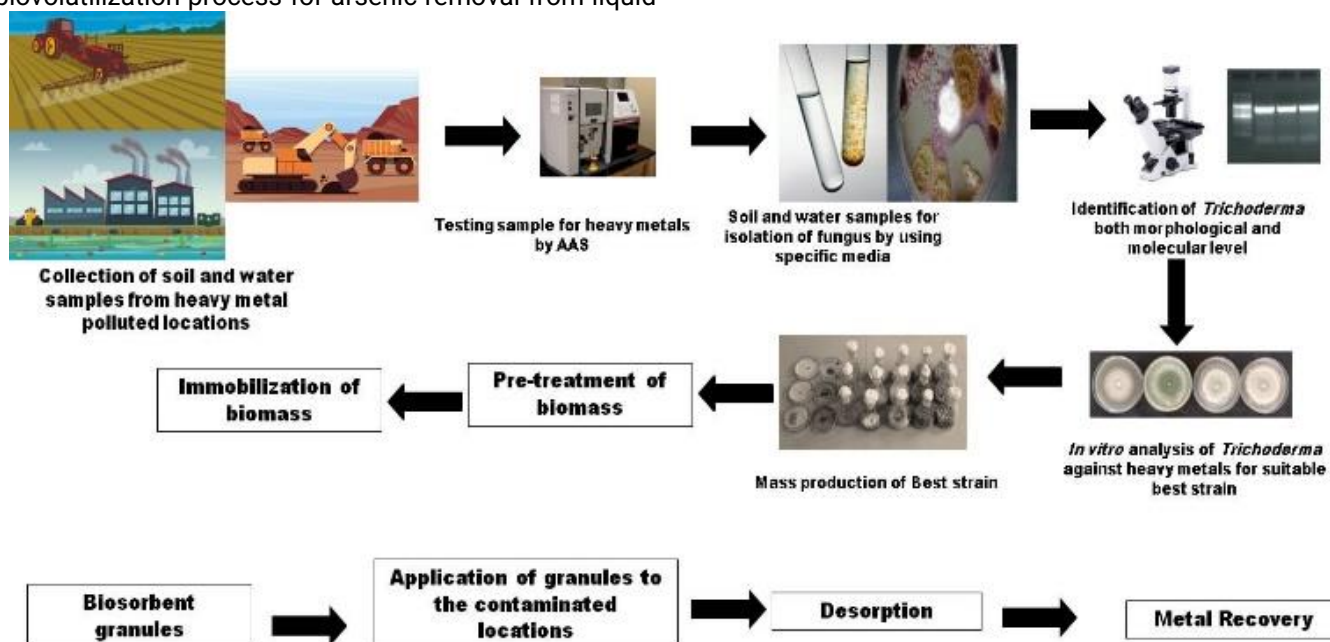


Figure 5. Events of biosorption process by *Trichoderma*

4.4 Biosorption Mechanism

Multiple methods of biosorption need to be clearly understood. In view of the complex structure of the microbe, the microbial cells can uptake metals in many ways, and they can be classified based on various criteria. Based on the cell's metabolism, the mechanism of biosorption can be classified into dependent and independent of metabolism, respectively. In the process of removal of metal from the solution, biosorption could be classified as

1. Extracellular
2. Sorption/precipitation and
3. Intracellular

When the movement of metal by the cell membrane results in intracellular accumulation, this is considered to be cell metabolism. This states that this method of

biosorption occurs only in the viable cells, which is also directly related to the defence system reactions on toxic metals. Meanwhile, in metabolism-independent biosorption, the uptake of metal is caused by physicochemical interaction. The major functional groups that lie on the cell surface hold the metal, which relies on physical adsorption, chemical sorption and ion exchange that doesn't rely on the cell's metabolism. The microbial biomass possessing cell walls is mainly composed of various compounds, namely polysaccharides, lipids, and proteins, that have the highest tendency to bind metals such as amino groups, carboxyl groups, phosphate and sulphate. It is independent in nature, reversible and rapid (Kuyucak & Volesky 1988).

Table 4. *Trichoderma* spp on remediation of pollutants

S. No.	Pollutants	<i>Trichoderma</i> spp.	Source
1.	Pb, Zn, Cd, Cu	<i>Trichoderma</i> spp.	Ayad et al. (2018)
2.	Pb, Zn, Cd, Cu, Ni	<i>Trichoderma</i> spp.	Tansengco et al. (2018)
3.	Poly aromatic hydrocarbons	<i>Trichoderma</i> spp.	Siddiquee et al. (2015)
4.	Polycyclic aromatic hydrocarbons	<i>Trichoderma</i> spp.	Argumedo-Delira et al. (2012)
5.	Pb, Cd	<i>T. asperellum</i> and <i>H. nigricans</i>	Maurya et al. (2019)
6.	Different types of organic solvents	<i>T. atroviride</i>	Oros et al. (2011)
7.	Pesticide group of Organophosphate such as dichlorvos	<i>Trichoderma atroviride</i>	Tang et al. (2010)

5. *Trichoderma* as a plant growth regulator

In natural soil, symbiosis occurs with crop plants and microorganisms present in soil. These microorganisms can be in two groups, namely PGPR and PGPF. PGPR is called in bacteria related to growth promotion and is as safe in fungi as PGPF. These PGPF and PGPR are reflected as regular biostimulants. *Trichoderma* spp is considered as PGPF. It is widely used for the management of phytopathogens as a biocontrol agent on a commercial scale (El-Komy et al. 2015). Some of the *Trichoderma* are considered endophytes due to its endophytic nature. It is present in various parts of plants, such as leaves and roots, and provides several benefits to host plants (Cummings et al. 2016). A symbiotic relationship occurs between the plant roots and *Trichoderma*. The beneficial bio-agent acts as a symbiont that colonizes the surface of roots and penetrates the root surface. *Trichoderma* secretes a number of secondary metabolites that activate several genomic and metabolic modifications in the host plant during their root initiations. The interaction between the *Trichoderma* and the host plant significantly improves plant growth

and development (Nur & Noor 2020). The application of *Trichoderma* spp increases plant nutrient uptake as the architecture of the root is improved with an increase in the length of primary and lateral roots. Enzymes such as cellulase, glucanases and xylanase are secreted by endophytic fungi, reducing the microbial cell function like nutrient absorption from the rhizosphere. These species of microbes are reported as an excellent example of PGPF due to its direct impact on plant growth promotion and improved crop production. Plants exert multiplex connections with the inhabitants in the rhizosphere. *Trichoderma* spp as PGPF in the soil ecosystem is suited for its high decomposer ability, its capability to boost up the nutrient uptake and the capability to adjust the rhizosphere. *Trichoderma* has significant advantages as its benefits can be obtained across a broad range of crops without any modifications to the crop varieties. In view of its mode of application, maximum benefits can be attained when the *Trichoderma* inoculums are applied at the early stage of crop growth. The growth promotion activities by *Trichoderma* vary from crop to crop or even within the genotypes of the crop.

Table 5. PGPF effect of *Trichoderma* spp. on crop plants

Crop	PGP effect	<i>Trichoderma</i> species/ strain	Reference
Bean	Root and shoot	<i>Trichoderma harzianum</i>	Pereira et al. (2014)
Cherry	Shoot and root	<i>Trichoderma harzianum</i>	Sofo et al. (2010)
Cucumber	Root, lateral roots	<i>Trichoderma harzianum</i>	Chang et al. (1986)
Cucumber	Shoot, chlorophyll and root.	<i>Trichoderma harzianum</i>	Yedidia et al. (2001)
Lettuce	Chlorophyll and root	<i>Trichoderma atroviride</i>	Colla et al. (2015)
Melon	Leaf number, root	<i>Trichoderma atroviride</i>	Colla et al. (2015)

Pepper	Root and shoot	<i>Trichoderma atroviride</i>	Colla et al. (2015)
Tomato	Stem, root	<i>Trichoderma harzianum</i>	Mastouri et al. (2012)
Tomato	Stem, root	<i>Trichoderma parareesei</i>	Rubio et al. (2014)
<i>Arabidopsis thaliana</i>	Shoot, root	<i>Trichoderma atroviride</i>	Garnica V et al. (2016)
Rice	Shoot, root	<i>Trichoderma asperellum</i>	Febriyono et al. (2018)

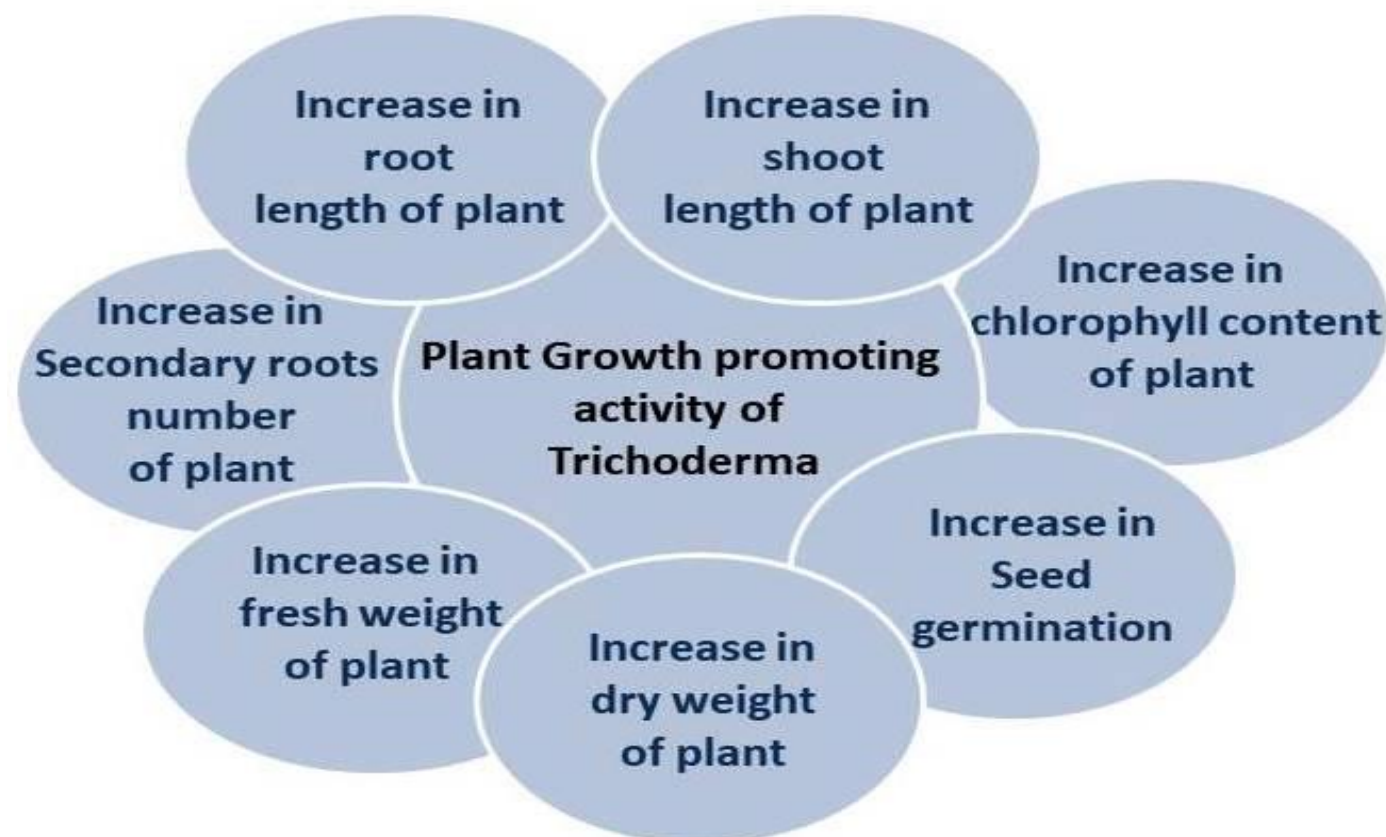


Figure 6. Plant growth promoting mechanism of *Trichoderma*

6 *Trichoderma* as nanoparticles

6.1 Nanoparticle biosynthesis by *Trichoderma*

The potential of fungi to produce a diverse spectrum of bioactive compounds, their propensity to accumulate metals, and their great ability to bind to cell walls and capacity to absorb significant amounts of metal make fungi more efficient than the majority of microorganisms in terms of efficiency (Guilger-Casagrande & Lima, 2019). *Trichoderma* species have been discovered to produce NPs that have antibacterial activity against a variety of microbes, including phytopathogens like *Aspergillus*, *Fusarium*, *Xanthomonas* and *Pseudomonas* (Bilesky et al. 2021). *Trichoderma* species for safe metal nano-particle production through mycogenic synthesis: *Trichoderma*

viride, *Trichoderma. asperellum*, *T. virens*, *T. reesei*, *T. longibrachiatum*, *T. fusant*, *T. atroviride*, *Hypocrealixii* and *Hypocreavirens*. The limitations used for mycosynthesis and special qualities of fungal strains must be tuned in order to obtain optimal mono-dispersity, durability and biocompatibility of the Nanoparticles. It was studied that the main aspects of monitoring the nucleation and successive construction of au Nanoparticles, shape, and size depend on fungal growth environments, time, beginning pH, temperature and substance concentration (Gemishev et al. 2019). Gold, ZnO, copper, selenium and Ag nanoparticles are among the primary NPs produced by *Trichoderma*, and each exhibits a variety of properties and antimicrobial activity.

Table 6. Trichogenic nano-particles and its application

NP	Strain	Shape	Size (nm)	Tested against	References
Ag	<i>Trichoderma</i> spp	Spherical to oval	5–50	<i>Sclerotinia sclerotiorum</i>	Tomah et al. 2020
	<i>T. harzianum</i>	Spherical	5–18	<i>Pyricularia oryzae</i> , <i>Alternaria alternata</i> and <i>S. sclerotiorum</i>	Consolo et al. 2020
	<i>Trichoderma</i> spp	Spherical	40–60	<i>F. solani</i> , <i>Fusarium semitectum</i> , <i>Fusarium oxysporum</i> , and <i>Fusarium roseum</i>	El-Wakil 2020
ZnO	<i>T. harzianum</i>	Fan structure	134–200	<i>Alternaria alternata</i>	Consolo et al.

				and <i>S. sclerotiorum</i>	2020
	<i>Trichoderma reesei</i> and <i>T. harzianum</i>	Hexagonal wuetzite and peaks	12–35	Xoo	Shobha et al. 2020
Au	<i>T. longibrachiatum</i>	Spherical and oval	102.93–123.99	<i>A. flavus</i> , <i>Aspergillus niger</i> and <i>A. fumigatus</i> , <i>P. aeruginosa</i> , and <i>S. aureus</i>	Elegbede et al. 2020
Se	<i>Trichoderma</i> sp.	Spherical and pseudo-spherical	WL-Go 20–220	Not tested	Diko et al. 2020
Si & Cu	<i>T. atroviride</i>	Irregular spherical	55.5 (Si), 56 (Cu)	<i>Poria hypolateritia</i> & <i>Phomopsis theae</i>	Natesan et al. 2021
a-Fe2O3	<i>T. harzianum</i>	No specified	207	<i>S. sclerotiorum</i>	Bilesky-Jose et al. 2021
Chitosan	<i>T. viride</i>	Nearly spherical	300	<i>R. solani</i> , <i>F. oxysporum</i> and <i>S. rolfsii</i>	Boruah & Dutta 2021

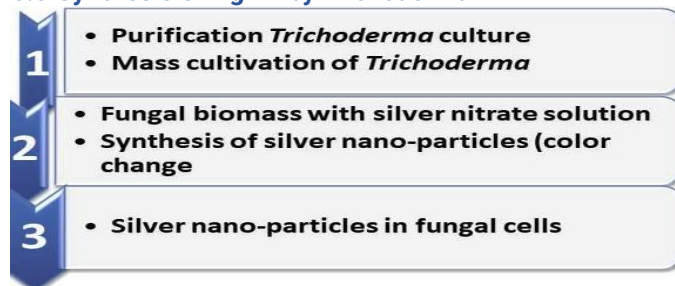
6.2 Silver nanoparticles

Silver nanoparticles (silver NPs) are in high demand because of their excellent bioactivity and comprehensive antibacterial properties against plant diseases (Tomah et al. 2020). As a result, using AgNPs can increase the effectiveness of agrochemicals while also lowering the need for biocides and pesticides (Dutta & Ahmed 2019). Both intracellular and extracellular processes are employed in the mycosynthesis of NPs, with the extracellular route being the more popular because it eliminates the need to remove NPs from the cells. To produce AgNPs, a decrease in the metal precursor (AgNO₃ salt) requires the biomolecules released by the fungus (Guilger-Casagrande & Lima 2019). One of the enzymes intricate in the reduction of metal ions is NAD-dependant nitrate reductase. For instance, extracellular enzymes produced by *T. reesei* can change silver ions into agglomerates of nanoparticles, with NADH-dependent nitrate reductase presence as the enzyme in charge of doing this. Noshad et al. (2019) found that the 1mM concentration produced silver nanoparticles with a lower size and greater antibacterial effectiveness. Using the *Trichoderma* isolate TCH 01, Ramos et al. (2020) tested reaction time and pH modifications for biosynthesis optimization and discovered that at pH five at the exposure of 9 days and produced smaller nanoparticles (150 nm) of silver nitrate and higher polydispersion rates. Similar efforts were made by Pal & Hossain (2020) to improve AgNP quality and yield by adjusting substrate concentration, pH and incubation time. According to their findings, pH 9, a 72-hour incubation time, and 2 mM AgNO₃ were the best conditions for producing spherical, monodisperse, and stable AgNPs. Due to the fact that the components are interdependent, the ideal conditions the writers mention may differ (pH, incubation time, and AgNO₃ concentration).

Research in this area has made it possible to comprehend several crucial mechanisms that occur during mycosynthesis. This enables the optimisation of the settings employed to produce particular AgNP properties, including dispersion, stability, and

biocompatibility. These earlier investigations collectively imply that the physicochemical circumstances of production, as well as the fungus culture, affect the properties of the produced NPs. Without the use of any hazardous reducing, capping, or dispersion agents, AgNPs were produced using a straightforward, green and environmentally acceptable method using *T. harzianum* cell filtrate. The extracellular filtrate from the entomopathogenic fungus *T. harzianum* is utilized to produce AgNP and has unique properties. For the first time, Saravanakumar & Wang (2018) reported on the synthesis of anisotropically organised AgNPs utilizing *T. atroviride* and explored their biological characteristics. The *Trichoderma* filtrate contains spherical NPs that are safe at low concentrations and biochemical that can bio-reduce silver nitrate (AgNO₃). Green AgNPs were created using exo-metabolites induced by chitin were isolated from the diverse and *T. fusant* Fu21 that is tolerant to stress by Hirpara & Gajera (2020). The development of compounds based on AgNPs and their fusion with fungicides should be the subject of more research. AgNPs produced extracellularly by biosynthesis may serve as transporters for various agrochemicals and naturally occurring bioactive compounds.

6.3 Synthesis of AgNP by *Trichoderma*



6.4 Zinc Oxide Nanoparticles

Among the nanoparticles that have been used most commonly in agriculture, ZnO nanoparticles stand out as being beneficial to both plants and soil microbiota. They are potent antibacterial agents and also have antifungal properties against *Botrytis cinerea*, *Rhizopus stolonifera*, *Fusarium spp.*, *A. niger* and *Penicillium expansum*. Shobha et al. (2020) used different *Trichoderma* isolates to

biosynthesize ZnONPs with crystalline structures free of contaminants, and these synthesized ZnONPs showed antibacterial effectiveness against the BLB of rice. They were able to create vast quantities of the ZnONPs with ease and sustainability. The zinc oxide nanoparticles they obtained had distinctive shapes of 12-35 nm. The several metabolites produced by *Trichoderma harzianum* and *T. reesei* (PGT5) monocultures and co-cultures were helpful in the synthesis of ZnO NPs. More effectively than monocultures, dual cultivation can stimulate the creation of novel metabolites. The optimum conditions for the production of *Trichoderma* based nanoparticles, T-D-glu-ZnO NPs, were achieved by employing a water extract of *T. harzianum* mycelial and their ability to conjugate D-glucan effectively can be verified by PACE and FTIR. They significantly reduced the growth of roundworms as well as the development of *Staphylococcus aureus* inside them (Saravanakumar et al. 2020).

6.5 Selenium nanoparticles

Selenium (Se) has positive effects on the metabolism and defence reaction of plants and animals in trace amounts as selenoproteins. Sea salts can, therefore, be substituted with Selenium nanoparticles. Hu et al. (2019) compared a conventional synthesis and a biosynthesis by *Trichoderma* regarding the synthesis of Selenium nanoparticles. They reported 60nm for the SeNPs produced by the TSNP approach, along with an irregular form that was probably brought on by the capping effect. In addition, the study found that the amount of amide materials, which serve as stabilizing agents, was higher in TSNP than in SNP (cappings). Diko et al. (2020), who investigated how pH affected the length of the inoculation process and the level of SeO₂ during the mycosynthesis of NP, suggest that the presence of alkane, alkene and alcohol functional groups in the SeNPs produced under the ideal conditions (pH of 8, 2mM SeO₂ concentration, 24 hours of SeO₂ inoculation, and *Trichoderma* sp.) served as cappings in the SeNPs synthesis reaction. The SeNPs produced were spherical and pseudo-spherical and measured 20–220 nm. In spite of the more investigations on AgNPs, the synthesis of SeNPs has received relatively little attention. Biosynthesized selenium nanoparticles (SeNPs) showed better effectiveness against pearl millet mildew disease (*Sclerospora graminicola*). when *T. asperellum* culture filtrate was used. SeNPs' biological activity was inversely correlated with their size. The biosynthesised selenium nanoparticles from *T. harzianum* JF309, when evaluated with standard available SNPs, showed antifungal activity was more on TSNPs, and they were found to be slightly larger.

6.6 Gold Nanoparticles

In the biomedical field, gold NPs are utilized as nano-drug carriers, diagnostic tools, antibacterial agents, and catalysts. For instance, a number of research have revealed AuNPs antibacterial action on several pathogens like *E. coli*, *S. aureus*, *P. aeruginosa*, etc. In addition, AuNPs biosynthesis is a less costly and environmentally benign substitute for electrochemical gold recovery processes like ion exchange resins and reverse osmosis (Nascimento et al. 2021). It is found that *T. harzianum* can biosorbent approximately 1,340

mg of gold per gramme of biomass in 180 minutes, and it can also produce NPs of spherical with less than 30 nm in size through mycosynthesis (Nascimento et al. 2021). A study was done on *T. harzianum* at three different levels of Au₂Cl₆ to find the ideal variables for mycosynthesis (0.25, 0.5, and 1mM). All of the settings produced AuNPs; however, the ideal conditions for producing smaller nanoparticles were 0.5 mM Au₂Cl₆, pH 7, and 38°C. These results showed that *Trichoderma*-mediated AuNP biosynthesis produces AuNPs with distinctive physical, chemical, thermal and optical properties that can be employed as a gold recovery method.

6.7 Copper nanoparticles

Using *T. asperellum* cell-free extract, copper oxide nanoparticles were produced (TA-CuO NPs). It was discovered that TA-CuO NPs had crystalline, spherical particles. The CuONPs had an average diameter of 100 nm and were available in sizes from 10 to 190 nm. The biosynthesis of *T. harzianum*'s NPs and the production of Copperoxide and Zinc oxiden nanoparticles were initially made known by Consolo et al. 2020. The production of biogenically created Silver, CuO, and ZnO NPs involved using *T. harzianum* cell filtrate as a reducer and stabilizer. The potential of silver and copper oxide for controlling phytopathogens was highlighted when the ZnO NPs tested against various target bacteria. Copper nanoparticles were successfully synthesized using *T. harzianum*. Cu and silica nanoparticles, when examined by TEM, EDAX analysis, and UV-vis spectrometry, were found to be aggregated, unevenly shaped, and range in size from 5 to 25 nm. According to reports, copper nanoparticles have an antibacterial effect against plant pathogens (Natesan et al. 2021). Their high surface-volume ratio properties can increase their antibacterial activity (Al-Hakkani 2020). *T. asperellum* forms CuONPs by encasing or decreasing the aromatic groups and amino of secondary metabolites.

6.8 Nanoparticles on *Trichoderma*

The phylogenesis usage of items that have various NP types suggests their impending entry into many ecosystems, such as aquifers or agricultural soils. According to some research, the presence of nanoparticles might cause changes in populations of microbes, possibly even influencing the positive relationships with crops. Cao et al. (2017) used AgNPs to demonstrate that the interaction between maize plants and arbuscular mycorrhizae is inhibited, resulting in a marked reduction in the rate of Alkaline phosphatase activity, the amount of phosphorus (P) that is readily available, and the nutrient status of the plants in relation to P. These findings imply that the type of nanoparticles, their quantity, and the microbes involved will vary significantly depending on their influence on plants. Experiments on how NPs affect plant-pathogenic fungi like *Fusarium*, *Aspergillus* and *Rhizopus* can reveal details about resistance mechanisms and suggest potential tactics that could be used by *Trichoderma* species to give them the benefit of tolerating higher concentrations of NPs than plant pathogens. However, research on how NPs affect fungus biocontrol is still in its infancy, and there isn't much known about it.

Toxicity

Evidence suggested specific partial effects on bacteria with regard to the impact of nanoparticles in soil, and the microbiota will likely recover over time. It is reasonable to conclude that this strategy represents the first step towards the prospective application of nanotechnology to prevent white mould in soybean crops because the silver nanoparticles-T had no adverse effects on soybean development. AgNPs produced by *T. atroviride* caused concentration-dependent cell modifications or harm or cytoplasmic compression. SNPs and TSNPs did not exhibit lethality or hypertoxicity for three cells when

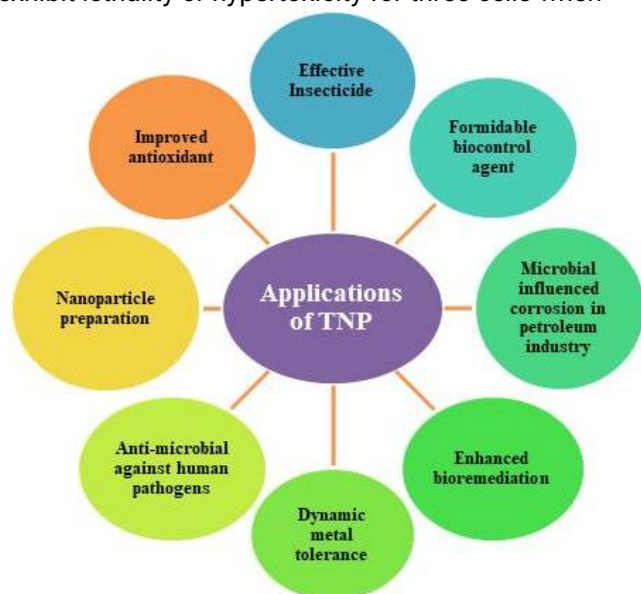


Figure 7. Application of *Trichoderma* nanoparticles

they were assessed for cytotoxic effects utilizing human viability and mortality. The lowest inhibitory concentration of green nano-formulations was found to be 20 g Ag/mL nano-formulations for the enhanced mycelium degradation activity of fungus (Hirpara & Gajera 2020). Utilising a number of cell lines, the cytotoxicity of FeONPs was studied, and the genotoxicity was measured using *Allium cepa* tests. When compared to controls, they did not affect cell viability, and the amounts employed did not result in changes to the mitotic index. Iron oxide nanoparticles were present, but they did not affect seed germination.

Potential Applications

It is possible to create mycogenic nanoparticles with a variety of particle size distributions. Reproducibility problems, uncontrolled shape of particles, dispersion, and size are present. To fully understand the ideal circumstances for producing NPs with the appropriate properties and to get improved outcomes when applied in many fields, including agro-nanotechnology, further research is nonetheless required. We are still in the early stages of developing novel nano-fungicides, nano-fertilizers, and nanosorbents produced by fungi and evaluating these nano-formulations to remediate industrial wastewater contaminated with heavy metals. As a result of the treatment approach, no NP residue may be released into the environment (Elamawi et al. 2018). For the time being, the toxicity of NPs continues to be a significant barrier, and this needs to be addressed further. Field tests of *Trichoderma*-based nanoparticles

are more important than ever to understand better interactions between nanoparticles, plants, and microbes, as well as toxicity issues.

7. Role of *Trichoderma* in industry

7.1 *Trichoderma* for industrial waste management by enzymatic degradation of agril waste

Demographics are correlated to waste; as the human population increases, the amount of garbage increases, too. Agricultural waste has become more of a concern, especially in agrarian nations like India, with the aim to increase production, which entails a large number of agricultural wastes. In India, agriculture contributes significantly to the economy. A variety of crops, particularly food grains, are grown there, leaving behind a large amount of residue once the profitable portions are harvested. The MNRE of India estimates that India produces 500 Mt or more of crop remains each year (NPMCR, 2019). According to the same report, the majority of this crop residue is used as feed, fuel, and for other home and industrial reasons. However, there remains a 140 Mt surplus, of which 92 Mt is incinerated each year. Utilizing agricultural waste for industrial use is done by employing micro-organisms. There are above 100 species of *Trichoderma* reported. Their enzymatic machinery comprises cellulose degrading enzyme cellulose, chitin degrading enzymes, chitinases, likewise glucanase and proteases, among others, for the decomposition of residual substrates in soil, lignocellulosic material in particular. Enhancement in the degradation of crop residue is due to several enzymes (Keswani et al. 2014). They have also been widely explored for their diverse characteristics and biotechnology applications.

7.2 Why is agricultural waste an environmental concern?

Burning crop residue is one of a farmer's improper disposal methods because it results in the release of greenhouse gases (GHGs) that contribute to global warming, higher levels of particulate matter (PM) and smog that pose health risks, a decline in the biodiversity of agricultural lands, and soil fertility (Lohan et al. 2018). A report on the burning of 98.4 Mt of crop residue during 2008–2009 by Jain et al. (2014) is presented in Table 7. It is estimated that CO₂ accounts for 91.6% of the total, and the remaining 8.43% was made up of 11% NMVOC, 5% NMHC, 2.2% NO, and 66% CO. Since the middle of October 2017, smoke from crop fires in Punjab and Haryana has spread to northern India and Pakistan. The smoke combined with fog, dust, and industrial pollution as the weather turned cooler in November created an unusually thick haze. In November, a lack of wind, which generally helps to disperse air pollution, made the issue worse for a few days. India is considered the second largest producer of rice, wheat, and other crops, which will leave behind large amounts of residue. Therefore, proper management of agricultural waste is sine qua none in the present scenario.

Table 7. Gases produced from crop residue burning (Jain et al. 2014)

Carbon monoxide	8.57 Mt
Carbon dioxide	141.15 Mt

Sulfur oxide	0.03 Mt
Nitrogen oxide	0.23 Mt
Ammonia	0.12 Mt
Non-methane VOC	1.46 Mt
Non-methane hydrocarbon	0.65 Mt
Particulate matter	1.21 Mt

7.3 Why is *Trichoderma* a degrader for agricultural waste?

Trichoderma spp. is ubiquitous in every ecological niche, endowed with different enzymatic components for their survival. In general, they produce a good number of lytic enzymes, cellulase, polygalacturonase, chitinase, etc., on the available substrate. Many *Trichoderma* strains recovered from the wild lack key lignocellulolytic enzymes for successful bio-conversion processes, particularly -glucosidases, which are considered key rate-limiting enzymes in the mechanism of cellulose degradation. For example, under cellulase-inducing circumstances, secreted-glucosidase production accounts for only around 1% of total *T. reesei* cellulase production, demonstrating that cellobiose hydrolysis is a rate-limiting step in the enzymatic digestion of cellulose (Chuang et al. 2016). Nonetheless, *Trichoderma* spp. familiarity to the farmer with their PGPF activity and biocontrol ability to plant against different types of stress; also seems likely to assist adoption for agricultural waste decomposition.

7.4 *Trichoderma* spp. in nature

Bhardwaj et al. (2017) asserted that lignocellulose comprises more than 60 % of plant biomass produced on earth, which arouses an assumption with the enzymatic capabilities of *Trichoderma* spp. that they involve in every decomposition process with their ubiquitous nature gives us a cue that they may involve in the cycle of life, i.e. from decomposition (death) to regeneration (life). However, four decades back, in 1973, Danielson and Davey found that each *Trichoderma* spp showed preferences in temperature and moisture content of the

soil. Like other microbes, *Trichoderma* is also sensitive to environmental factors. Although *Trichoderma* spp. is known as an aggressive competitor, its ability is species-dependent.

7.5 Enzymatic activity of *Trichoderma* spp.

In general, crop residue comprises 10 % dry mass with lignocellulosic materials (10-25%). *T. virens* is able to break down both of these substances due to its ability to produce enzymes. Compost contaminated with *T. virens* exhibits more xylanase and cellulase activity than uncontaminated compost. These processes ultimately hasten the breakdown of cellulose and hemicellulose, which aids in hastening the decomposition procedure. Experiment on EFB from the oil palm industry inoculated with *Trichoderma* spp. found greater N, P, and K over control (Siddiquee et al. 2017). To maximize cellulosic biofuel production at a competitive price, researchers studied the development of the *Trichoderma reesei* enzymes cellulase and xylanase with substrates such as wheat bran, rice straw, and rice husk. Sawdusts that contain toxic substances can be degraded by the application of *T. viride*. Furthermore, *T. asperellum* and *T. harzianum* have been shown to be a promising option for lignocellulose degradation in vegetable refuse (Prawiti et al. 2021). Additionally, its capacity to detoxify harmful inorganic substances, including polycyclic aromatic hydrocarbons, has been demonstrated (PAH). The breakdown of organic material is accelerated by *T. harzianum*, *T. viridae* and *T. hamatum* by the production of cellulase. Several species also produce lignin peroxidase and laccase for lingo-cellulosic material, which helps in lignin degradation (Dabhi et al. 2017). As a result, *Trichoderma* spp. is considered a possible natural decomposition agent capable of producing quality compost in aerobic or micro-aerobic environments with less oxygen. The majority of crop residues need more systematized and scientific disposal methods; conversion into compost is an ideal alternative.

Table 8. Degradation of various organic compounds by *Trichoderma* spp.

Species	Major enzyme	Substrate	References
<i>Trichoderma viride</i>	Cellulase	Rice bran	Nadagouda et al. 2016
<i>T. asperellum</i>	laccase and peroxidase	Polycyclic aromatic hydrocarbons	Zafra et al. 2015
<i>Trichoderma reesei</i>	Cellulase and Hemicellulase and Xylanase	Paddy straw	Taherzadeg-Ghahfarokhi et al. 2019
<i>Trichoderma viride</i> , <i>Trichoderma harzianum</i>	Manganese lignin, etc.	Lignin	Dabhi et al. 2017
<i>Trichoderma viride</i>	Cellulase	Waste of flowers, kitchen waste (vegetables) etc.	Ahuja & Bhatt et al. 2018

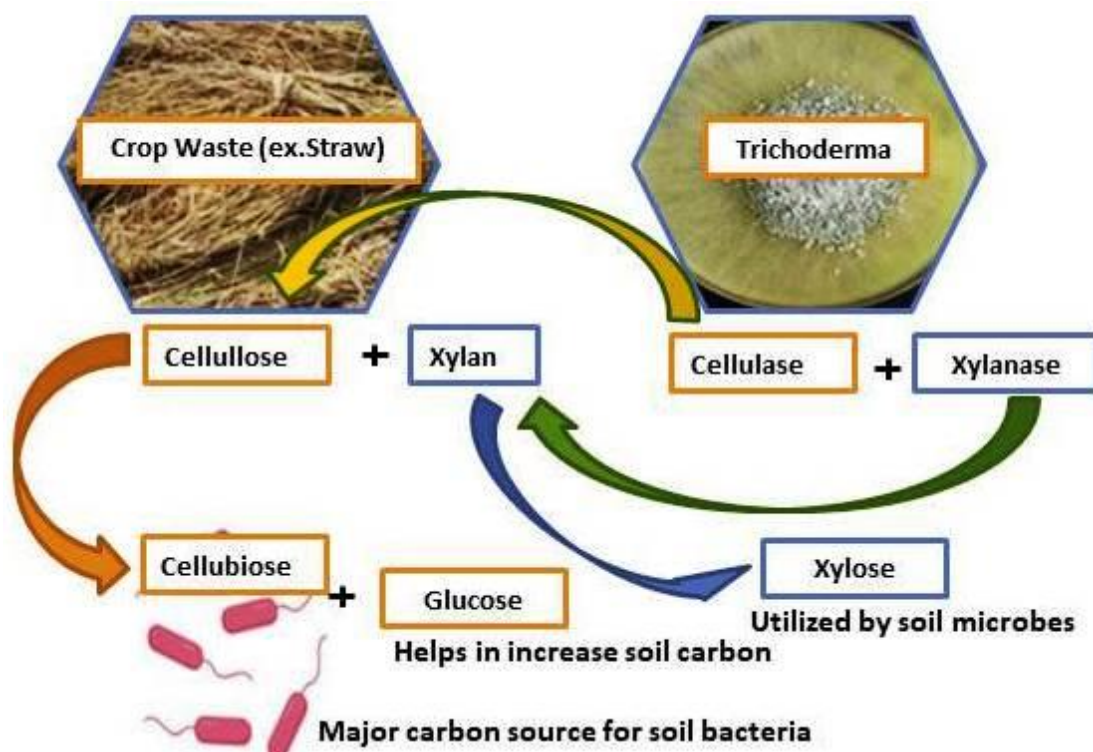


Figure 8. Enzymatic degradation of Agri-waste by *Trichoderma*

8. Role of *Trichoderma* in drug discovery

Diverse metabolites secreted by *Trichoderma* species have immense potential as a source of novel drug discovery. An extensive review by Zhang et al. (2021) mentioned 203 compounds respectively isolated from

Trichoderma that have therapeutic value and can be explored for novel drug development in future. An indicative list of biological activities associated with different metabolites isolated from *Trichoderma* spp is given in Figure 9 below.

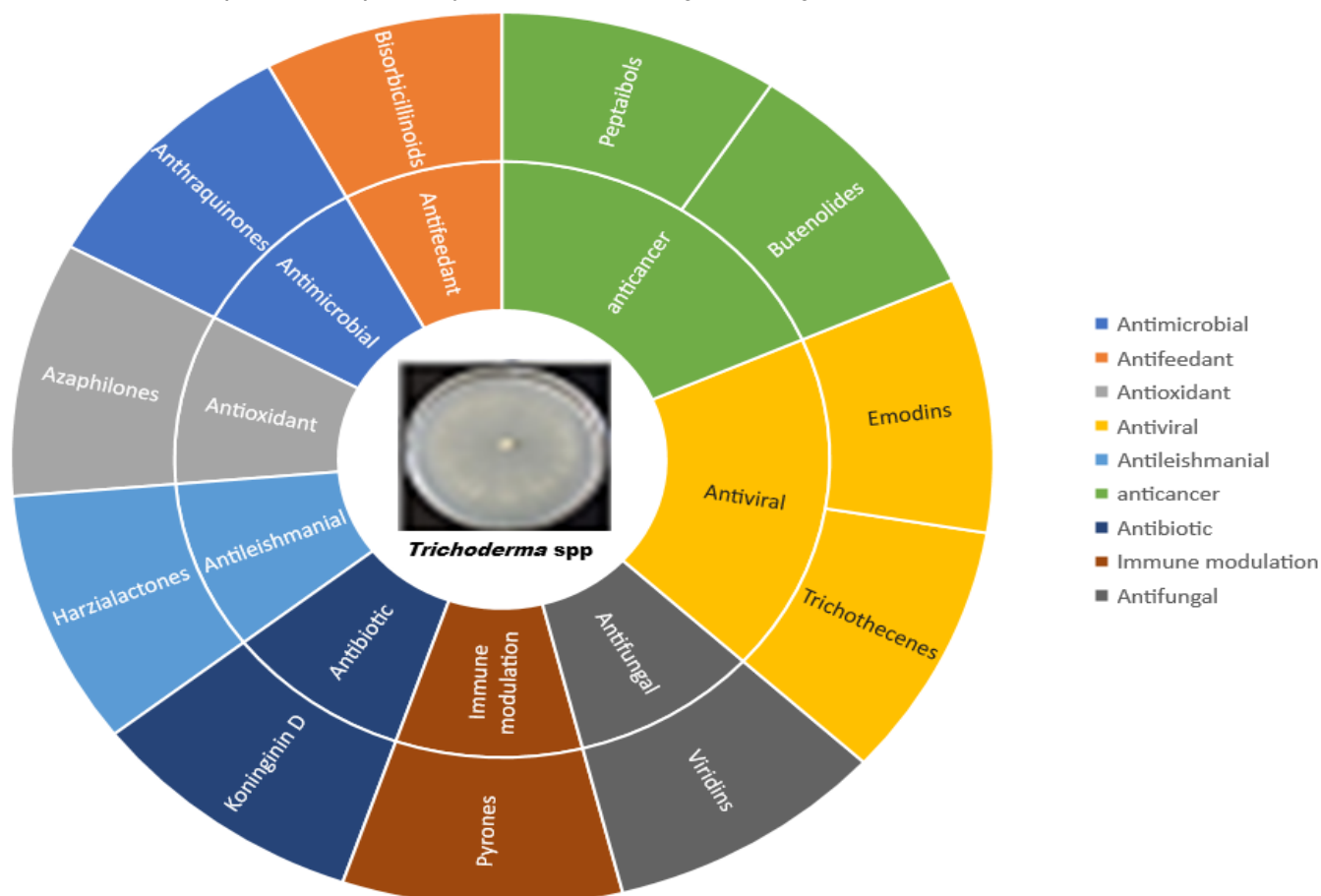


Figure 9. Biological Activities of *Trichoderma* metabolites

8.1 Antimicrobial properties

The antimicrobial properties of the *Trichoderma* spp metabolites (including antiviral, antifungal, antimicrobial and antibiotic activities) broadly depend on the ability of these compounds to simulate the actions of organic acids or non-polar compounds owing to their chemical structures. The metabolites, primarily terpenoids, anthraquinones, steroids, polyketides, have been reported to have antimicrobial properties (Sharma et al. 2017). Another plausible mechanism by which these compounds impart their antimicrobial properties is by modulating the defense of host plants through improved availability of nutrients from the soil. The range of other molecules that are deployed by *Trichoderma* spp to counter the growth of phyto-human pathogens includes lytic enzymes, peptaibols, volatile and non-volatile low molecular weight compounds.

8.2 Antioxidant Activities

The metabolite arsenal of *Trichoderma* spp includes low molecular weight volatile compounds such as pyrones, peptaibols, harzianopyridone, etc., exert their radical scavenging activities, leading to a decrease in the reactive oxygen species (ROS) followed by a reduction in oxidative stress. This helps the host cells delay the process of ageing as a reduction in ROS aids in maintaining the cell wall structure, reducing damage to DNA and mitochondria. Similar mechanisms have been reported by Konappa et al. 2021.

8.3 Anticancer properties of *Trichoderma* metabolites

The *Trichoderma* metabolite that has been widely implicated in the anticancer properties against a range of cancer ailments like cancer (breast, lung, colon, bladder), melanoma and sarcoma cancer xenografts is the enzyme Chitinase that belongs to the hydrolases category (EC 3). This enzyme is known to catalyse the transformation of chitin to its monomeric components in organisms ranging from bacteria to fungi (Martinez-Zavala et al. 2020). It is a fact that normal mammalian cells do not contain chitin. This allows the use of chitinase as a potential drug against cancer cell lines. The regular cells will not be damaged by chitinase activity, but the cell surface of the cancerous cells will be significantly damaged. Another study validated the earlier reports of L-lysine oxidase (EC 1.4.3.14) derived from *T. viride* as an active agent exhibiting antitumour and cytotoxic activity in breast cancer. Oxidation of L-lysine (an essential amino acid) by L-lysine oxidase is the primary method by which this enzyme exhibits its anticancer effect. Studies have reported a 70 % decline in L-lysine levels in the blood caused by L-lysine oxidase derived from *Trichoderma cf. aureoviride* is sufficient to suppress the growth of tumour cells in mice. L-lysine oxidase reduces the levels of not only lysine but also L-arginine, which induces cell viability inhibition, apoptosis and reduction of tumour growth. Researchers have proposed cationic amino acids as an effective tool for cancer treatment (Okita et al. 2021).

The third mechanism by which metabolites derived from *Trichoderma* function as anticancer agents is by employing Chitosan-oligosaccharides (COS). COS has the potential for human health to be used as an anticancer and anti-cholesterol. It is an oligomer of β -(1

– 4) linked d-glucosamine produced on deacetylation and hydrolysis of chitin by enzymes such as chitosanases and chitinases. Recently, 331 enzymes that have chitinase activity have been shown in the uniprot database for *Trichoderma harzianum* (<https://www.uniprot.org/>). The presence of electrostatic charges on COS disrupts the permeability of the tumour cells, and the simultaneous expression of tumour factors is a possible mechanism by which COS effectively regulates the proliferation of cancer cells (Liaquat & Eltem 2018).

8.4 Ant leishmanial Activities

Leishmaniasis is a transmissible disease caused by a parasitic protozoan from the *Leishmania* genus. The parasite is carried to the mammalian hosts by female phlebotomine sandflies. The disease has varied clinical severity from asymptomatic mild symptoms to death in severe cases. Humans, wild mammals, and domestic dogs are the hosts of the parasite. In recent research published by Lopes et al. (2020), the ethanolic extract of *Trichoderma asperelloides* had leishmanicidal action against the promastigote and amastigotes of *Leishmania amazonensis*. The low molecular weight fractions of the ethanolic extract led to the morphological disintegration of mitochondria flagella of promastigotes. It also led to an increase in the lipid body, disorganization of cytoplasmic microtubules, acidocalcisome formation, and intense vacuolization of the cytoplasm of amastigotes. These ultrastructural changes in the developmental forms of the parasite severely impact the survival possibilities of the pathogen and aid in controlling the disease.

8.5 Immune modulation Activities

A recent study by Oliveira-Mendonça et al. (2022) has demonstrated the immune modulation activities of spores of *Trichoderma stromaticum*. They postulated that when mice are exposed to *Trichoderma asperelloides* spores, there is a marked decrease in neutrophil counts in the peripheral blood and the peritoneal cavity. Further, the spores of *Trichoderma stromaticum* produce inflammation in the mice's lungs, leading to a reduction in interferon γ (IFN- γ) and interleukin – 10 (IL-10) cytokine storm, restrained ROS generation, and control the receptors of microbes. Their study elucidated that the interaction of human peripheral neutrophils and spores of *T. stromaticum* led to reduced release of neutrophil extracellular traps (NETs), leading to immune modulatory effects. The micro-RNA production by spores of *Trichoderma stromaticum* seems to be the plausible mechanism by which these organisms modulate the NET formation.

Conclusion

Trichoderma spp. is a beneficial microbe considered to be one of the wonder microbes that have diverse applications in supporting human life. The dual benefits of *Trichoderma* in plant growth promotion and biological control of plant pathogens have been known and utilized extensively with limited success due to constraints of extrinsic factors like soil, host species, inherent properties like viability of the spores, and region specificity of the *Trichoderma*. As most of the benefits of *Trichoderma* are mediated through the wealth of

secondary metabolites it secretes, the most judicious exploitation of this organism can be realised through novel technologies that can isolate the metabolites in purified form and further use these metabolites for diverse applications in the field of agriculture, food industry, and novel drug improvement. The commercial exploitation of *Trichoderma* secreted secondary metabolites needs to be developed, and future targeted research in this field can help humanity abundantly.

Author's Contribution

Bireswar and LK Mishra: Conceptualization, Data organization, Investigation, Writing – original draft; S M Haldhar: Revision of manuscript; PK Sarangi: Data organization; Kota Chakrapani: Heavy metal write-up; R Poorva Sandhya: Nanoparticles; W Tampakleima: Foliar diseases; Rimamay Konjengbam: Insect management; BijetaTh: PGPF and Zarzoliana Ralte: Industrial waste.

Declaration of Interests

The authors have no conflict of interest to declare.

Data Sharing

All relevant data are within the manuscript.

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