



Microbial endophytes: application towards sustainable agriculture and food security

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Abstract

Microbial endophytes are ubiquitous and exist in each recognised plant species reported till date. Within the host plant, the entire community of microbes lives non-invasively within the active internal tissues without causing any harm to the plant. Endophytes interact with their host plant via metabolic communication enables them to generate signal molecules. In addition, the host plant's genetic recombination with endophytes helps them to imitate the host's physicochemical functions and develop identical active molecules. Therefore, when cultured separately, they begin producing the host plant phytochemicals. The fungal species *Penicillium chrysogenum* has portrayed the glory days of antibiotics with the invention of the antibiotic penicillin. Therefore, fungi have substantially supported social health by developing many bioactive molecules utilised as antioxidant, antibacterial, antiviral, immunomodulatory and anticancerous agents. But plant-related microbes have emanated as fountainheads of biologically functional compounds with higher levels of medicinal perspective in recent years. Researchers have been motivated by the endless need for potent drugs to investigate alternate ways to find new endophytes and bioactive molecules, which tend to be a probable aim for drug discovery. The current research trends with these promising endophytic organisms are reviewed in this review paper.

Key points

- Identified 54 important bioactive compounds as agricultural relevance
- Role of genome mining of endophytes and “Multi-Omics” tools in sustainable agriculture
- A thorough description and graphical presentation of agricultural significance of plant endophytes

Keywords Endophytes · Secondary metabolite · Plant adaptation · Industrial potential · Biological activity

Introduction

Plant endophytes are endosymbiont microbes that spend a part of their life cycle inside a living host without inflicting any signature of their existence (Suryanarayanan 2017; Van der Meij et al. 2017). Endophytes boost the tolerance of

host plants to adverse environmental conditions both directly and indirectly. Plant growth-promoting microorganisms (PGPMs), which include plant growth-promoting bacteria (PGPBs) and plant growth promoting fungi (PGPFs), also play an eminent role in plant growth and tolerance to a range of environmental stresses (Dubey et al. 2020). PGPMs possess the potential to fix atmospheric nitrogen (N₂), promoting functioning of plant via the formation of ACC deaminase, siderophore release, phytohormone biosynthesis and phosphorus solubilisation. Thus, it is critical to explore additional strategies other than the genetic improvement of plants to increase their resistance to abiotic stress (Lata et al. 2018). Numerous studies have approached this issue differently, highlighting the need to adopt endophytic microbes that are advantageous to plants and positively influence plant microbe interactions (Lahlali et al. 2021). These favourable plant microbe interactions may best achieve the world's food

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requirements. During these interactions, plants and microbes form cooperative as well as advantageous partnerships, which contribute towards the tolerance of host plants to different challenges comprising toxins, heavy metals, drought, salt, nutritional challenges, and high temperatures. Bioconsortia acts as a biofertilizer, improving agricultural productivity at the lowest possible cost. Nowadays, the emergence of bioconsortia has reignited global excitement and has the potential to contribute to a new green revolution (Caruso et al. 2020) (Fig. 1).

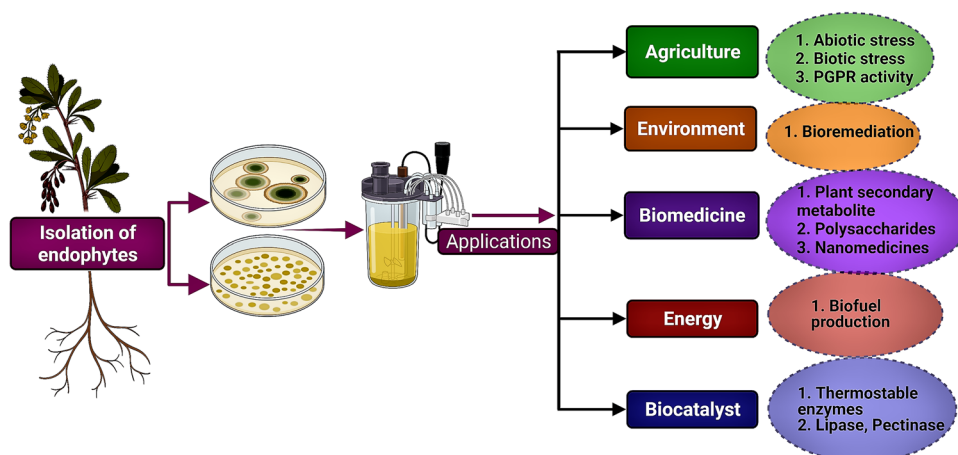
Horizontal gene transfer mainly explains how plants and microbes are developed by the movement of genetic information from donor to different recipient. The endophytic fungi have the ability to produce same class of secondary metabolites through genomic clustering of genes and are subsequently transferred to other symbiotic species. Whereas, the amino acid synthesis mechanisms in fungi and plants are appeared same but seemed different in secondary metabolite biosynthetic pathways (Dwibedi et al. 2021). Clustering secondary metabolite genes conserves genetic order with the help of biosynthetic enzymes found in a particular genomic arrangement. These inducing factors discover that the rise of secondary metabolites in plants and fungi are similar and indicate that endophytic fungi can contribute to secondary metabolite production management (Sharma et al. 2016). Through the endophytic interactions, the secondary metabolites like paclitaxel, Hsp90 inhibitors (Palwe et al. 2021), resveratrol (Dwibedi and Saxena 2018, 2019, 2020; Dwibedi et al. 2021) and camptothecin (Ruan et al. 2021) were synthesised in plants.

Subcultures were repeated under axenic monoculture conditions to restrict secondary metabolite production additionally, partial or complete secondary metabolite synthesis routes in plants might be associated with endophyte-plant interactions (Alam et al. 2021). Researchers have shown a keen interest in the communication between endophytic

fungi and plants to improve secondary metabolite production. Numerous secondary metabolites that possess therapeutic potential have been commercialised due to endophytic interactions (paclitaxel, camptothecin and podophyllotoxin) (Mitra et al. 2021; Dwibedi and Saxena 2018). Combining an endophytic fungus (*Phialocephala fortinii*) with the rhizomes of *Podophyllum peltatum* resulted in a two-fold increase in podophyllotoxin production (Stierle et al. 1999; Suryanarayanan 2017). Similarly, by establishing contact between *Cyanea acuminata* and endophytic fungi, it was possible to increase the accumulation of camptothecin and its two analogues (9-methoxycamptothecin and 10-hydroxycamptothecin) (Lorence et al. 2004). By establishing a relationship between *Acalypha indica* and endophytic fungi, we could boost the production of azadirachtin A and B (Kumar 2020). Endophytic fungi's interaction with plant tissues boosts secondary metabolite production asymptotically. This interaction resulted in the development of several bioactive compounds (podophyllotoxin, paclitaxel, camptothecin, artemisinin, cannabinoids, hypericin, isopestacin, morphine and pestacin) that were cytotoxic, antibacterial, insecticidal, anticancer and antioxidant (Strobel and Daisy 2003; Strobel et al. 2004; Strobel 2011; Dwibedi and Saxena 2018; Kumar 2020; Dwibedi et al. 2021).

Hamayun et al. (2017) inoculated *Porostereums padiceum* AGH786 in *Glycine max* under saline conditions. This colonisation reduced the effect of salinity by decreasing the levels of Jasmonic acid and Abscisic acid and increasing the levels of Gibberellic acid. Gul Jan et al. (2019) described the interaction of endophytic strain *Yarrowia lipolytica* with *Zea mays* in saline conditions. Positive effect of interaction was observed in saline conditions, where interaction promoted the improvement in plant growth attributes such as leaf relative water, chlorophyll content, levels of oxidative enzymes and chlorophyll content. Eslahi et al. (2020) suggested plant growth promotion in *Jerusalem artichoke*

Fig. 1 Current state applications of endophytes



plants with the production of siderophores by endophytic strains. During the study, *Trichoderma koningii* ST-KKU1, *Macrophomia phaseolina* SS1L10 and SS1R10 endophytic strains were responsible for siderophores production. Cellulose and xylanase producing enzymes were found to be expressed in *Betula pendula* because of colonisation with *Trichoderma camerunense* strains (Eslahi et al. 2020). The production of cellulose and xylanase is desirable for biofuel production, which act as sustainable biorefinery as alternative to pre-treating feedstock with chemicals. *Arachis hypogaea* plants growth was increased due to their association with *Phomopsis liquidambari* which was responsible for expressing the new laccase gene. This expressed laccase exhibited application in agriculture by promoting growth of plant and reducing phenol concentrations in soil and in industrial sector as it was thermostable as well as acid-tolerant (Falade et al. 2021). *Fusarium solani* endophytic fungus in *Dendrobium officinale* host plants produced polysaccharide galactoglucan. This polysaccharide was found to be beneficial as a food for treating patients having hypo-immunity as it enhances immune response. *Fusarium solani* species in host plant *Fritillaria unibracteata* produced a polysaccharide which has different composition that includes rhamnose, arabinose, mannose, glucose, pyranose, galactose and xylose. This polysaccharide has inhibitory activities for cell proliferation and is efficient antioxidant (Zeng et al. 2019). *Trichoderma asperellum* in *Lactuca sativa* plant hosts were found to be biocontrol agents for fungal species *Curvularia aerea* and *Corynespora cassiicola* responsible for causing lettuce leaf spot disease. *Trichoderma* sp. produced volatile compounds which triggered the production of beta-1,3-glucanase and chitinase activity which is responsible for degradation of pathogen fungus cell wall. It also plays a significant role in photosynthesis by improving chlorophyll content and increasing plant growth. In *Solanum lycopersicum* var. *Cerasiforme*, four different strains of endophytes *Hypoxylon xanthochroum* produced volatile organic compounds such as monoterpenes and sesquiterpenes. This volatile organic acid inhibits the growth of *F. oxysporum* in host plants (Khunnamwong et al. 2020). *Streptomyces albidoflavus* OsiLf-2 is endophytic strain isolated from *Oryza sativa* which produces metabolites against pathogenicity causing fungus *Magnaporthe oryzae*. It suppressed the growth of pathogen as well as obstructed appressorial formation in them. They also produce various agriculture sustainable compounds such as siderophores, antimicrobial compounds, phytohormones and cell wall lytic enzymes. They also stimulate the activation of enzymes, expression of salicylic acid and build-up of hydrogen peroxide as defence responses (Gao et al. 2020).

Nowadays, maximum research has been conducted in the area of endophytic interaction with their host plant for

their application towards plant growth promotion research (PGPR). But the present study highlights how endophytes research deciphers the complicated network of physical, genetic, metabolic and biochemical connections among plants, their related endophytic microorganisms and the environment. The present study discusses how these communications influence the composition of plant related endophytic microbiota and influence favourable features like nutrient acquisition and plant health, as well as knowledge gaps and future initiatives. Endosymbiosis' effect on the metabolism, gene expression of host and other physiological characteristics is also well validated in giving resistance to biotic and abiotic stressors. The other aspect of our novelties is how endophytes synthesise host-derived secondary metabolites and their significant responsibilities are in disease management and treatment. This review also concentrates on how the potential bacterial endophytes can promote plant growth and biotechnological applications in the agricultural field. Moreover, a worthy discussion on omics approaches in this review is another portion of add-on technology that is now well accepted for sustainable bioremediation, plant growth promotion and biocontrol. Aside from that, this review elucidates how plant-associated microbiota contributes to the long-term sustainability of agricultural growth and food safety (Fig. 1).

Plant hosts for endophytes, their distribution within plants and their density

Endophytes may invade a wide range of plant species and organs (Bacon and White 2000). Endophytes are known to colonise nearly all plant species examined thus so far (Zhou et al. 2020), including field crops, horticulture crops, perennial trees and medicinal plants (Zhou et al. 2020). Many plants' root systems, leaves, stalks, fruits, and seeds have been separated from endophyte population density. On the other hand, varies depending on the plant component. For example, the largest concentration of endophytes is usually found in plant roots, followed by stems and leaves. The concentrations of endophytes in other plant components, such as fruits, flowers (Schulz and Boyle 2006) and seeds, are substantially lower than in stems. Endophytes may be difficult to detect in other plant parts due to their low population density (De Souza et al. 2021). While some have claimed that high endophytic population densities are linked to dangerous bacteria, healthy plants have been found with up to 10^{10} colony forming units (CFU) of endophytes per gram of tissue (Vega Hurtado 2020). Plant variety, host development stage variation and isolation techniques used are some of the other factors that influence endophyte density (Compant et al. 2021). Even the common technique of surface sterilisation used to isolate endophytic microbes can have an impact on

their population density and recovery from host plant tissues, because some of the agents used to surface sterilise plants can penetrate plant tissues, causing endophyte communities to be damaged (Schulz and Boyle 2006) (Fig. 1) (Table 1).

In the beginning, investigations on endophyte communities were conducted in vitro using culturable endophyte communities, with unculturable endophytes being ignored (Dubey et al. 2020; Strobel and Daisy 2003). Endophyte activity in vitro does not necessarily fulfil the same duties as in natural settings, making such studies difficult (Elnahal et al. 2022). Furthermore, researchers' capacity to accurately analyse plant endophyte dynamics was impeded by the challenges associated with maintaining slow-growing taxa as well as mandatory microbial species, which are notoriously difficult to separate due to their distinct culture demands (Ludwig-Müller 2015). Because cultivable endophytes account for less than 1% of total endophytic microorganisms, they cannot be used to characterise the activities of whole plant endophyte communities (Lugtenberg et al. 2016). As a result, genetic and biological technologies originally developed to better understand and investigate uncultivable bacteria are now being effectively employed for the analysis of endophyte community diversification and function in plants (Sarhan et al. 2019). For example, by combining highly discriminating 16S and 18S rRNA sequences with modern "omics techniques", determining the phylogenetic structure and function of both culturable and nonculturable endophyte communities in a short amount of time and at a low cost has become substantially easier (Caruso et al. 2020). Even the resolution of microbiological taxonomy may be modified to match the needs of each researcher in several ways (Fig. 1; Table 1).

Factors determining the composition of endophytes

Plant endophyte communities are structurally and functionally heterogeneous for a variety of reasons. There are various factors like host plant, growth stage, plant organ, environmental factors, soil and management practices and presence of plant pathogens which are responsible for the distribution pattern of the endophytes.

Plant host

The plant's genus is a well-known element that influences the composition of endophytic microbial communities (Chalot and Puschenreiter 2021). Furthermore, a current study suggests that genetic differences across species within the same plant genus may alter the endophyte bacterial population's composition. For example, T-RFLP fingerprinting and 16S rRNA sequences revealed considerable variations

in the endophyte bacterial populations of two sweet pepper varieties (Whipps et al. 2008; Bodenhausen et al. 2014; Truyens et al. 2015). Similarly, Chen et al. used the internal transcribed spacer region (ITS) of nuclear ribosomal DNA to identify changes in fungal diversity among 10 *Dendrobium* species in a study of fungal endophytic diversity (Chen et al. 2013). Endophytic microbial species found in any one plant host that does not indicate that these microorganisms are host-specific. The methods by which a plant host can impact a variety of endophyte communities are unknown, and further research is required to interpret these mechanisms (Bacon and White 2000; Chen et al. 2013; Strobel 2018).

Plant growth stage

The growth stage of plants is another factor that is highly linked to endophyte communities. Different phases of sugar beet (*Beta vulgaris* L.) seedling growth influenced bacterial endophyte communities using Illumina sequencing of the 16 s rRNA gene. This transition occurred when the plants began to form tuber and rosette structures, as well as during the accumulation of sucrose in the taproots (Masenya et al. 2021). The sugarcane plants' phenological stage most likely caused variations in the number of these important microbial groups. Based on physical and physiological characteristics, endophytic microbial species differ between immature and mature winter wheat (*Triticum aestivum*) plants (Schulz and Boyle 2006; Lugtenberg et al. 2016). According to the scientists, these discrepancies were caused by plants' smaller and weaker vegetative tissues, which gave less endophyte colonisation during the winter and more possibilities for cold-temperature fungus and other less competitive microorganisms to colonise plant tissues. Endophytic growth rates climbed inside plant tissues throughout the summer and spring, when plant biomass was actively expanding, diminishing the competitive dominance of a few endophyte species present throughout the winter (Schulz and Boyle 2006; Suryanarayanan 2017).

Plant organs

Various organs within the same plant may sustain different endophyte groupings. When using RAPD and 16S rRNA sequence analysis to define maize endophyte communities, researchers (Johnston-Monje and Raizada 2011) revealed that the diversity of *Proteobacteria* was larger in roots than in shoots. These bacteria were also found in plant rhizospheres, indicating that they may have originated in the soil. This finding might help to explain why they were found in greater abundance in roots than in shoots (Ludwig-Müller

Table 1 Endophytes with potential agricultural relevance

S. no	Bacterial endophytes	Host plant	Agricultural relevance	References
1	<i>Bacillus cereus</i> and <i>B. subtilis</i>	Leaves of <i>Teucrium polium</i>	Plant growth promoting properties	(Hassan 2017)
2	<i>Bacillus</i> sp. and <i>Pseudomonas</i> sp.	Buds of <i>Malus domestica</i>	Apple shoot growth, cellular redox balance, and protein expression under <i>in-vitro</i> conditions	(Tamošišinė et al. 2018)
3	<i>Enterobacter</i> sp. strain PDN3,	Cuttings of <i>Populus deltoides x nigra</i>	Endophyte-assisted phytoremediation of Trichloroethylene	(Doty et al. 2017)
4	<i>Pseudomonas stutzeri</i> A15	Rhizosphere and endosphere of <i>Oryza sativa</i>	Plant growth promoting properties	(Pham et al. 2017)
5	<i>Serratia grimesii</i> BXF1 (Transformed strain for ACC deaminase activity)	<i>Pine pinaster</i> , <i>Solanum lycopersicum</i> and <i>Cucumis sativus</i>	Co-inoculation of <i>Serratia grimesii</i> BXF1 with <i>Rhizobium tropici</i> CIAT 899 promotes early nodulation and growth of common bean	(Tavares et al. 2018)
6	<i>Enterobacter</i> sp.	<i>Eleusine coracana</i>	Suppressing <i>Fusarium graminearum</i> in plant tissues and reduction of deoxynivalenolmycotoxin	(Mousa et al. 2016)
7	<i>Bacillus cereus</i> strain 65	<i>Sinapis arvensis</i> L	Antifungal	(Pleban et al. 1997)
8	<i>Bacillus</i> sp., <i>Achromobacter</i> sp., <i>Alcaligenes</i> sp.	<i>Helianthus annuus</i> L	Plant growth and development	(Forchetti et al. 2007)
9	<i>Bacillus mojavensis</i> RRC 101	<i>Bacopa monnieri</i> L	Biocontrol of <i>Fusarium verticillioides</i>	(Snook et al. 2009)
10	<i>Rhizobium leguminosarum</i>	<i>Oryza sativa</i> L	Biofertilization, increase rice yield	(Yanni and Dazzo 2010)
11	<i>Rahnella</i> sp. and <i>Pseudomonas</i> sp.	<i>Musa</i> L	Bio-fertilisation	(Ngamau et al. 2012)
12	<i>Streptomyces</i> sp. GMKU 3100	<i>Oryzasativa</i> L	Promote plant growth	(Rungin et al. 2012)
13	<i>Enterobacter</i> sp. FD17	<i>Zea mays</i> L	Enhancement of maize yield	(Naveed et al. 2014)
14	<i>Agrobacterium fabrum</i> , <i>Acinetobacter radioresistans</i> , <i>Brevibacillus brevis</i> , <i>Bacillus cereus</i> , <i>Bacillus subtilis</i> , <i>Paenibacillus barengoltzii</i> , and <i>Burkholderia cepacia</i>	<i>Pulicaria incisa</i>	Exhibited variant tolerances to salt stress and showed high efficacy in indole-3-acetic acid (IAA) production in the absence/presence of tryptophan	(Fouda et al. 2021)
15	<i>Bacillus cereus</i> , <i>Pseudomonas otiitidis</i> , <i>Pseudomonas</i> sp.	Soybean root tissues	Plant growth-promoting (PGP) traits, biocontrol potential, and drought stress alleviation	(Dubey et al. 2020)
16	<i>Staphylococcus pasteurii</i> strain MBL_B3 and <i>Ralstonia solanacearum</i> strain MBL_B6	<i>Corechoriso litorius</i>	Bioinoculants	(Haidar et al. 2018)
17	<i>Bacillus</i> , <i>Lysinibacillus</i> , <i>Enterobacter</i> , <i>Stenotrophomonas</i> , <i>Lelliottia</i> and <i>Pseudomonas</i>	<i>Euphorbia trigona</i> mill	Drought tolerance and growth promotion in tomato	(Eke et al. 2019)
S. no	Fungal endophytes	Host plant	Agricultural relevance	References
18	<i>Alternaria</i> , <i>Cladosporium</i> and <i>Fusarium</i>	<i>Limonium tetragonum</i> , <i>Suaeda australis</i> , <i>Suaeda maritima</i> , <i>Suaeda glauca</i> (Bunge), and <i>Phragmites australis</i>	Plant growth-promoting (PGP) activity	(Khalmuratova et al. 2020)
19	<i>Agaricus bisporus</i> , <i>Mycolepto discus</i>	<i>Vanda cristata</i>	Auxin synthesis, phosphate solubilisation, ammonia synthesis, and elicitor growth test for understanding their growth-promoting effect	(Chand et al. 2020)
20	<i>Fusarium</i> , <i>Alternaria</i> , <i>Acremonium</i>	<i>Santalum album</i>	Biological diversity, antibacterial activities and the plant growth-promoting traits	(Liu et al. 2020)
21	<i>Alternaria</i> , <i>Didymella</i> , <i>Fusarium</i> and <i>Xylogone</i>	<i>Sophora flavescens</i>	Plant growth-promoting (PGP) activity	(Turbat et al. 2020)
22	<i>Fusarium</i> sp. R13 and R6, <i>Colletotrichum alatae</i>	<i>Dendrobium moniliforme</i>	Plant growth-promoting (PGP) activity	(Sha et al. 2018)

Table 1 (continued)

23	<i>Alternaria</i> , <i>Fusarium</i>	<i>Phragmites australis</i> , <i>Suaeda australis</i> , <i>Limonium tetragonum</i> , <i>Suaeda glauca</i> (Bunge), and <i>Suaeda maritima</i>	Plant growth-promoting (PGP) activity	(Khalмурatova et al. 2020)
24	<i>Trichoderma</i> strains A14 and A3	<i>Celitica gigantea</i>	Growth promotion in tritordeum	(de Aldana et al. 2021)
25	<i>Trichoderma</i>	<i>Triticum aestivum</i> L	Plant growth-promoting (PGP) activity	(Ripa et al. 2019)
26	<i>Serendipita indica</i>	Not provided	Plant-growth-promoting-microbe (PGPM)	(Osman et al. 2020)
27	<i>Penicillium</i> , <i>Alternaria</i> , and <i>Aspergillus</i>	<i>Ephedra pachyclada</i>	Plant growth-promoting properties	(Khalil et al. 2021)
28	<i>Fusarium redolens</i> (RF1), <i>Phialemoniopsis cornearis</i> (SF1), and <i>Macrophomina pseudophaseolina</i> (SF2)	<i>Coleus forskohlii</i>	IAA production	(Mastan et al. 2019)
29	<i>Phoma</i> sp, <i>Fusarium</i> sp.	<i>Glycyrrhiza glabra</i>	Plant growth promoting hormone, Indole acetic acid production	(Arora et al. 2019)
30	<i>Alternaria elegans</i> , <i>Aspergillus lanosus</i> , <i>Penicillium commune</i> , <i>Penicillium crustosum</i>	<i>Phaseolus vulgaris</i> L	Produce indole-3-acetic acid (IAA) and different hydrolytic enzymes such as amylase, cellulase, protease, pectinase, and xylanase	(Ismail et al. 2021)

2015; Lugtenberg et al. 2016). Based on BLAST searches of the ITS sequence in the NCBI GenBank database and phylogenetic analysis, other research with *Dendrobium* plants found that the amount and composition of fungal endophytes had changed throughout plant tissues (Lugtenberg et al. 2016). *Fusarium* sp., for example, makes up 68.2% of the root fungal endophyte population, 20.6% of the stems and 11.2% of the leaves. In addition, many fungal isolates were found in stem and leaf tissues but not in roots, including *Collectotrichum* sp. The bulk of endophytic fungus colonisation is of the roots of *Dendrobium* plants rather than the stems and leaves. Endophyte community composition discrepancies across roots, shoots and stems are frequently due to environmental and biological variances across plant tissues. Another study found that orchid leaves and roots exposed to similar levels of light and air had the same endophytic fungal population composition (Yuan et al. 2009; Chen et al. 2010, 2011; Parthibhan et al. 2017).

Climate

Endophyte populations can be influenced by environmental factors that are not dependent on the plant type or organ. It has been shown, for example, that climatic variations between geographic regions, or even within the same region, influence plant endophyte groupings (Zarraonaindia et al. 2015; Peay et al. 2016). In one study, endophyte communities in adult teak tree (*Tectona grandis*) leaves were altered according to rainfall patterns, with certain species only appearing during rainy seasons (Patturaj et al. 2021). Another study used 16 s rRNA gene libraries to examine the endophyte composition of chilled and non-chilled sweet pepper (*Capsicum annum*) plants (Mantzoukas and Lago-geannidis 2019). On the other hand, meteorological circumstances have a smaller impact on root endophyte diversity than on aerial plant tissues (Latz et al. 2021). Endophyte assemblages in the roots appear to respond only to long-term environmental changes caused by precipitation and high CO₂ concentrations (Singh et al. 2021a, b). Using agar plating and morphological identification, 45 microbial taxa were recovered from tree roots immersed in a river, but only 31 species were recovered from non-submerged tree roots of the same tree (Stroheker et al. 2021). Aerial hyphomycetes were also more prevalent in submerged roots, suggesting that soil moisture has an impact on root endophyte populations. Root endophyte diversity is influenced more by variations in the quality and quantity of photosynthates and other metabolites inside roots, as well as root turnover rate and soil microbial community composition, than by external environmental conditions (Lugtenberg et al. 2016).

Characteristics of the soil and management practices

An essential element influencing the makeup of plant microbiomes is the composition of resident soil microbial communities, which is influenced by both soil type and management approaches (Schulz and Boyle 2006). It has been proven, for example, that soil physical and chemical parameters such as pH, texture, moisture, temperature and macro and micronutrient availability all impact the composition of root endophyte communities (Schulz and Boyle 2006). This has been well documented in the case of significant microbial species, including dark septate endophytes and arbuscular mycorrhizal fungi (AMF) (Pieterse et al. 2014), both of which are acknowledged for their potential to solubilise phosphorus which makes it more available for uptake by host plant. It was established that these microbial groups increased in plant hosts cultured in low phosphorus soils after dyeing roots and evaluating AMF and DSE abundance using the magnified intersect approach (Mburu et al. 2021).

Endophyte diversity can be influenced by various management strategies, either directly or indirectly, through changes in the bulk soil microbial population (Tang et al. 2020). When root endophytes were separated using culture-dependent methods and identified using morphological criteria, Schulz and Boyle (2006) found that cutting and clearing forest trees within rows altered the variety of root endophytes. Another study found that the composition of fungal taxa differed between grapevines managed organically and those grown using integrated pest management techniques, using an automated ribosomal intergenic spacer to characterise endophytes in *Vitis vinifera* (Deyett and Rolshausen 2020). Changes in soil physical and chemical characteristics, which alter bulk soil microbial communities, as well as direct effects caused by the presence of different organic substrates required for soil microbe support and pesticide application, could explain differences in endophyte diversity associated with such alternative management practices.

Presence of plant pathogens

Plant endophyte populations have been reported to be affected by both general and specialised plant disease infections. For example, researchers employed 16S rRNA-based denaturing gradient gel electrophoresis (DGGE) to estimate the diversity of endophytic *Pseudomonas* sp. in potato (*Solanum tuberosum*) tubers infected or not with *Erwinia carotovora*. Rai et al. (2021) discovered distinct changes in *Pseudomonas* population diversity in response to pathogen infection in *Atrorseptica*. Plants resistant to *Erwinia* infection

had a wider range of *Pseudomonas* sp., which was surprising. This might be related to differences in the antagonistic behaviour of *Pseudomonas spoverallii* in resistant plants. It might be linked to chemical and physical alterations in endophyte environments caused by pathogen-induced activation of plant defence mechanisms (Schulz and Boyle 2006; Parthibhan et al. 2017; Suryanarayanan 2017).

Why and how do endophytes generate host derived secondary metabolites?

Endophytes can benefit in two ways by mimicking their hosts' metabolites. To begin, the endophyte's ability to synthesise secondary metabolites from the host may help it compete with other invading fungi, such as other endophytes and illnesses (Dwibedi et al. 2021). Secondly, it may increase plant defences against pest invasions or disease, giving the endophyte indirect fitness benefits by improving the host's fitness (Strobel and Daisy 2003; Strobel et al. 2004). However, two key requirements must be met as prerequisites for this to happen. To begin with, the endophytes which generate the metabolites of host ought to be resistant to it, specifically when the metabolite is toxic to cells, like CPT or taxol. Moreover, if fungi generate metabolites in order to battle with other invading plant pathogenic fungi, these metabolites have to be transported across the mycelial cell membrane and cell wall into the intercellular spaces of plant tissue in order to efficiently combat and surpass the invading fungi. Some earlier reported literature gives an idea about the possibility of gene transfer between endophyte and host which can help in producing secondary metabolites in the host cell (Sudhakar et al. 2013; Joo et al. 2021). In plant, taxol biosynthetic pathways follow various transformative chemical stages following several cellular compartments like plastids, endoplasmic reticulum, cytoplasm and additionally involvement of total 19 genes. But it was reported that the genetic similarities in fungal endophytic gene sequence are similar up to 99% and 97% to *T. x media* and *T. wallichiana* species respectively (Zhang et al. 2009; Sudhakar et al. 2013). Similarly, in the case of CPT, 13 genes are involved in the biosynthetic mevalonate pathway. Out of which 11 genes seem homologous to CPT producing endophytic fungus, *Fusarium equiseti* isolated from *Nothapodytes nimmoniana* (Bhalkar et al. 2016; Ding et al. 2017). Thus, considering these studies, it can be stated that by acquiring genes from host plant endophytes may find genetic activation in biosynthetic routes or epigenetic modification to produce bioactive secondary metabolites (Sudhakar et al. 2013; Meena et al. 2019). We are looking to see whether there is any evidence in nature to back up these assumptions (Table 1).

Bioactive secondary metabolites from endophytes and their significance

The renewed interest in nature derived bioactive compounds has relatively low side effects than the available synthetic drugs. Notably, endophytes residing in the plant tissue are more promising source of new compounds believed to be biosynthesized from the host due to their diversity of occurrences, much explored after the invention of a taxol producing fungus in the bark and needles of the Northwest Pacific yew tree. The highly efficient, low toxic anticancer natural drug paclitaxel (Taxol®) is produced by more than 200 fungal strains most commonly like *Taxomyces andreanae* and *Phoma medicaginis* of the original host plants *Taxus brevifolia* and *Taxus wallichiana* respectively. However, since 1993, taxol producing species *Taxomyces andreanae* was a commercial breakthrough in attaining robust industrial production. Biotechnology-based toolkits using tissue or cell culture or genetic engineering techniques to enhance the taxol productivity or other bioactive metabolites are well focused and used commonly to achieve the desired yield for the economic profit. The fermentation and enzymatic conversion of substrates into bioactive compounds are to be followed to enrich the productivity of secondary metabolites from endophytic strains. The isolation of endophytes is mainly conducted using surface sterilisation, vacuuming, and cell culture techniques and their identification is performed by morphological and molecular phylogenetic technology (Rustamova et al. 2020). Podophyllotoxin, a natural potent antimetabolic agent and tubulin polymerase inhibitor, and a few of its analogues are produced from two endophytic strains *P. peltatum* and *Phialocephala fortinii* and also isolated from numerous non-host plants like *Alternaria* sp. and species of *Juniper* (Kumari et al. 2017). Artemisinin, an FDA approved antimalarial drug, was isolated from medicinal plant *Artemisia annua* in green fluorescent protein (EGFP) expressing endophytic *Actinobacteria* YIM 63111 strain. It was reported that there was an increase in productivity of artemisinin content from 1.99 to 2.57 mg/g as endophytes get involved in promoting the development of glandular trichomes which helps in upregulating the gene expression in artemisinin biosynthetic pathways (Li et al. 2012; Zheng et al. 2021). Vitexin, apigenin-glycosylated flavones, that was isolated from endophytic fungus from the leaves of *Cajanus cajan* (pigeon pea) has shown remarkable antioxidant activity with reported EC₅₀ value 164 µg ml⁻¹ (Guet et al. 2018a, b). Camptothecin, a pentacyclic pyrroloquinoline alkaloidal drug, is isolated from endophytic fungus *Trichoderma atroviride*, produced mainly by *Camptotheca acuminata* and *Nothapodytes foetida* (Pu et al. 2013). *Ginkgo* tree is the major source of different classes of bioactive secondary metabolites like flavonoids,

terpenoids and most common diterpenoid lactones from the leaves and barks of *Ginkgo biloba* by fungal fermentation. Bioactive anticancer metabolites chaetomugilins A and D and chaetoglobosins A and C were isolated from the fungal endophytic strain *Chaetomium globosum* from the sterilised leaves of *G. Biloba* and these compounds have also shown inhibitory activity against the brine shrimp (Qin et al. 2009). Cui et al. reported that the Ginkgolide B, a diterpenoid tri lactone, was identified from fungal fermented isolates of endophytic fungus *Fusarium oxysporum* that originally grow in the host natural resource the root bark and leaves of *Ginkgo biloba* (Cui et al. 2012). Earlier, (+)-cryptosporiopsin, 4-epi-ethiosolide, (-)-mycorrhizin A, (R)-mellein and 2-methoxy-4-hydroxy-6-methoxymethyl-benzaldehyde are some fungicidal and herbicidal secondary metabolites which were isolated from endophytic *Pezizula* species (Schulz et al. 1995). Secondary metabolites, like mellein, gliovictin acetate, peniprequinolone, 4-(2-hydroxyethyl) phenol and gliovictin and p-hydroxybenzaldehyde, were reported from the culture of two endophytic fungi E3 and *Penicillium janczewskii* isolated from the phloem of *Prumnopitys andina* de Laub. Earlier, Kusano et al. reported bioactive compound peniprequinolone from *Penicillium* cf. *simplicissimum* which have shown a nematocidal effect against nematode *Pratylenchus penetrans* (Schmeda-Hirschmann et al. 2005). By the approach of biotransformation with the addition of 0.01% w/v curcumin, calebin-A, a curcuminoid compound, was studied from endophytic fungal strain *Ovatospora brasiliensis* of host medicinal plant *Curcuma caesia* rhizome. The bioconversion of curcumin to calebin-A was occurred in a time dependent manner at temperature 37 ± 0.5 °C for 7 days (Majeed et al. 2019). Eugenol, allyl chain-substituted guaiacol, is commonly called aromatic clove oil extracted from clove, cinnamon, bay leaf, etc. used to treat toothache, root canal therapy and periodontal therapy. Eugenol is renowned for diverse pharmacological activities, especially for antimicrobial and antioxidant activities, anaesthetic and anti-inflammatory properties. This volatile compound is isolated from several endophytes like endophytic fungus *Annulohyphoxylon stygium* BCRC 34,024, *Neopestalotiopsis* and *Diaporthe* sp. as endophytic fungi associated with *Cinnamomum loureiroi*, bacterial endophytes isolated from *Mentha piperita*. Its derivative methyl eugenol is produced by endophytic fungus in *Alternaria* species from *Rosa damascena*. Along with eugenol, lauric acid, myristaldehyde and caprylic acid were also reported from the *Neopestalotiopsis* sp. and *Diaporthe* sp. (Tanapichatsakul et al. 2019). Grigoletto et al. reported that fumiquinone B isolated from ethyl acetate fractions of endophytic fungi *Neopestalotiopsis* sp. from the plant *Begonia fischeri* Schrank was observed active against the plant pathogen *Diaporthe phaseolorum* (Grigoletto et al.

2019). Kaaniche et al. isolated fungal endophytic strain T12 from the stem bark of *Rauwolfia macrophylla*. The extract was fractionated and three bioactive secondary metabolites, 2'-deoxyribolactone, hexylitaconic acid and ergosterol, were isolated through column chromatography using Sephadex LH-20. These isolated compounds exhibited high free radical scavenging ability and also displayed antimicrobial and acetylcholinesterase inhibitory activity (Kaaniche et al. 2019). The high affinity iron chelating siderophore, herquilineB and antibiotic 3-O-methylfunicone were three bioactive metabolites isolated from the endophytic strain of *Talaromyces pinophilus* from the host medicinal plant *Arbutus unedo* (Vinale et al. 2017). Xiao et al. reported the first time three new secondary metabolites, one of them is a yellow gum pyrone derivative named Pysarone A and rest two are red coloured naphthalenone derivatives (3-demethoxyl-fusarnaphthoquinone B and (2S, 3S, 4S)-8-dehydroxy-8-methoxyl-dihydronaphthalenone) from the endophytic fungus *Fusarium* species (Xiao et al. 2018). Three new secondary metabolites Atrichodermones A–C

were reported from endophytic fungal strain *Trichoderma atroviride* which was isolated from the bulb of *Lycoris radiata*. However, none of these three observed remarkable cytotoxicity or anti-inflammatory activity (Zhou et al. 2017). In 2020, Guo et al. reported nine polyketides from which four new secondary bioactive metabolites (Pestalotiones A–D) and five known compounds, isosulochrin dehydrate, 3,8-dihydroxy-6-methyl-9-oxo-9H-xanthene-1-carboxylate, chloroisosulochrin, isosulochrin and pestalotether D, were isolated from the crude extracts of endophytic fungus *Pestalotiopsis theae* (N635). The new compounds pestalotiones A and B have shown good antioxidant activity compared with others (Guo et al. 2020)(Figs. 2, 3 and 4a) (Tables 2 and 3).

Wang et al. reported six new alkaloids bearing phenethylamine (PEA) discolins A and B, dispyridine, dispyrrolopyridine A and B, and dispyrrole were isolated from bacterium *Tenacibaculum discolour*. The isolated compounds dispyrrolopyridine A and B have shown strong activity against gram-positive bacteria like *Bacillus subtilis*, *Mycobacterium*

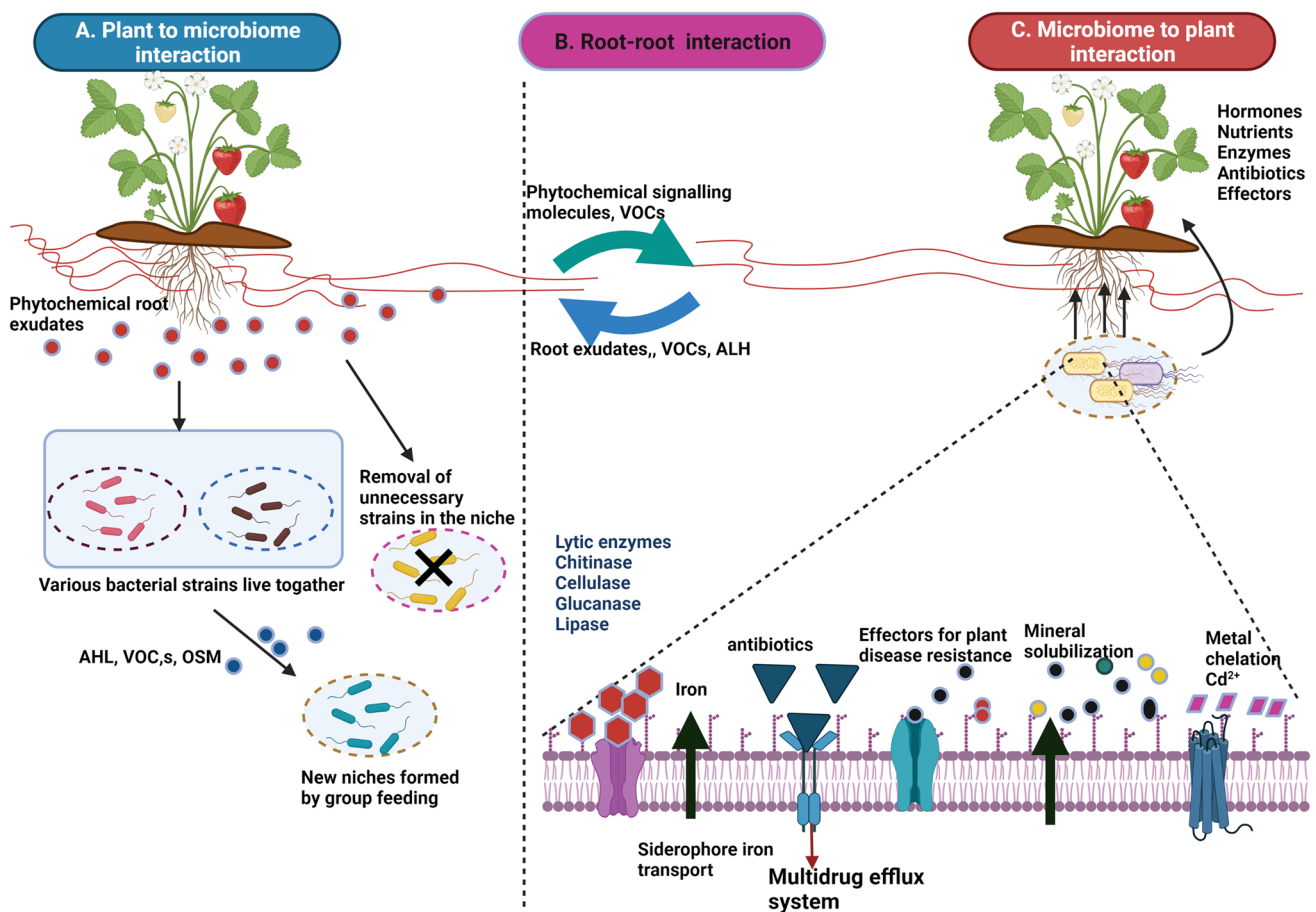


Fig. 2 Multifarious interaction of plant and microbiome **a** plant to microbiome interaction; **b** root and root interaction; **c** microbiome to plant interaction

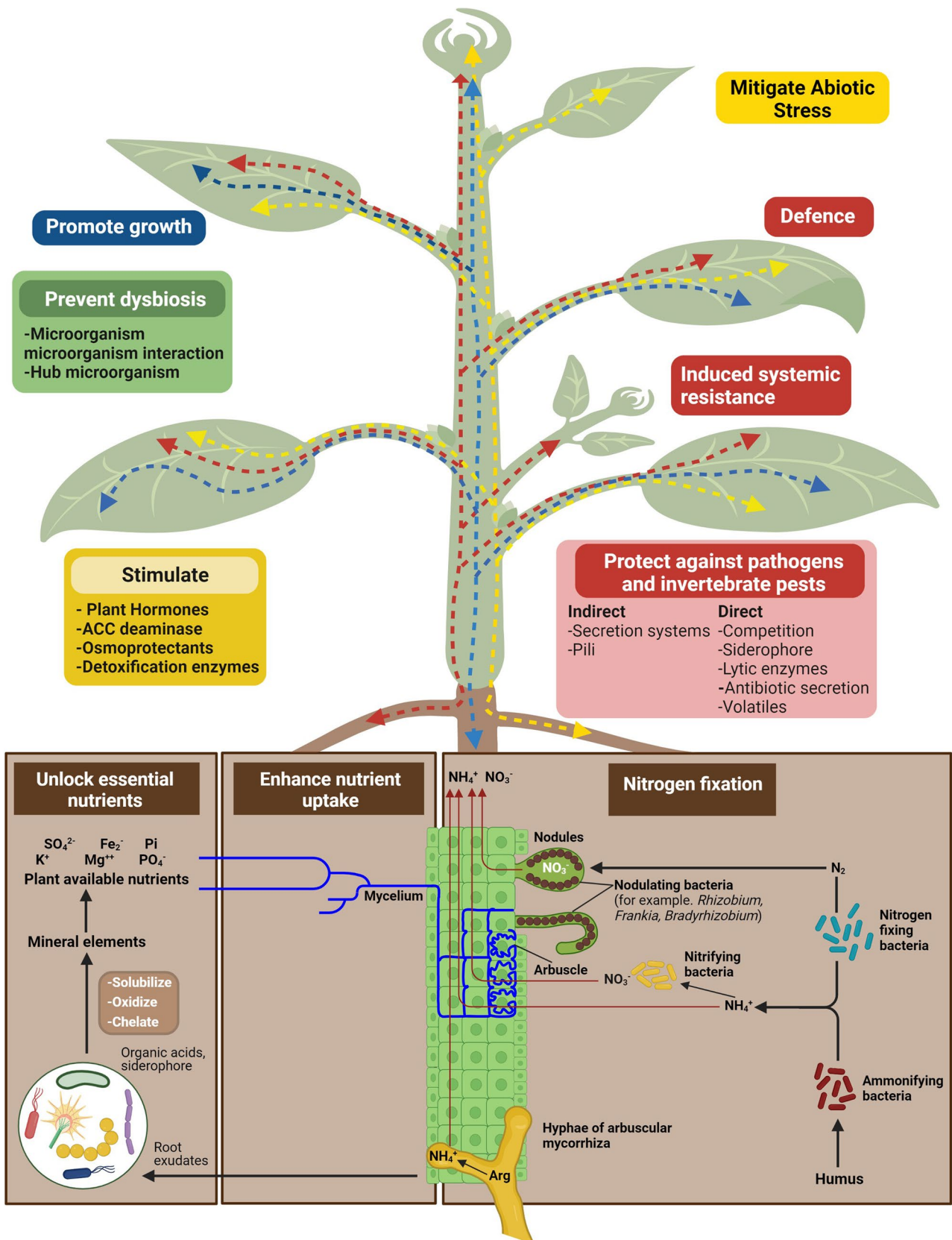


Fig. 3 Mechanism of endophytes to mitigate abiotic and biotic stress in plant and their role in plant growth promotion

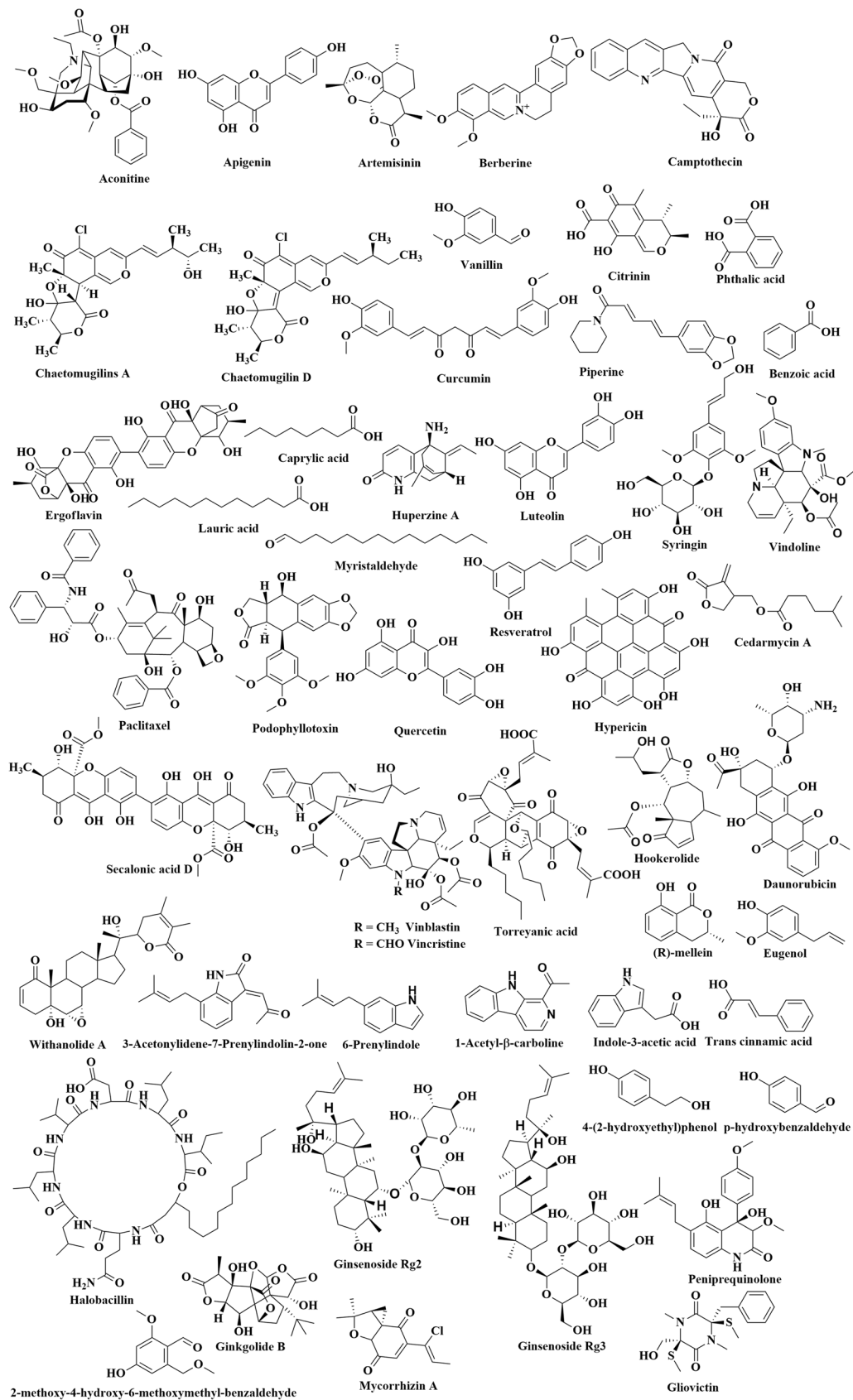


Fig. 4 a and b Bioactive secondary metabolites produced by endophytic fungi and endophytic bacteria

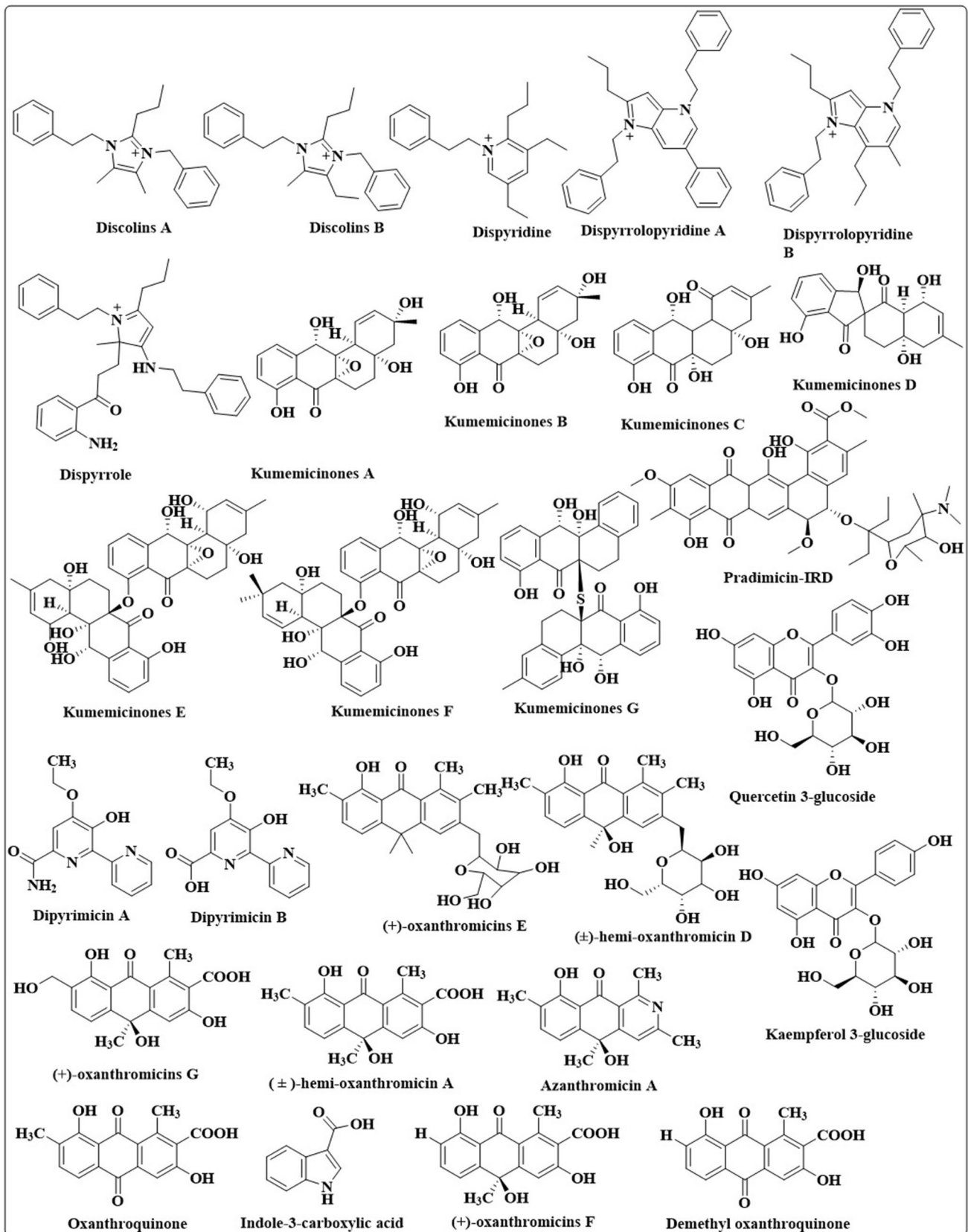


Fig. 4 (continued)

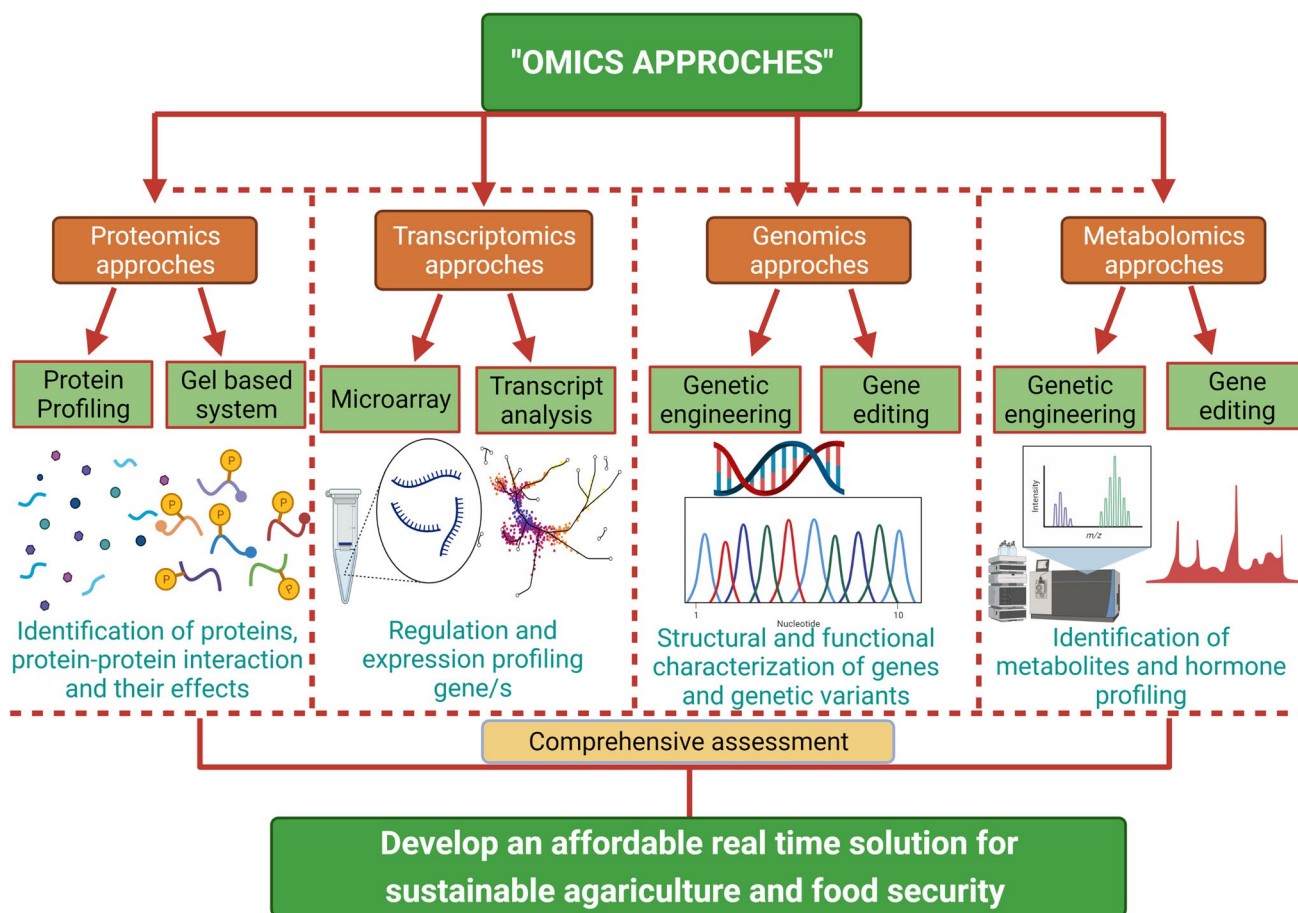


Fig. 5 Various “OMICS” approach used in sustainable agriculture and food security

smegmatis, *Listeria monocytogenes* and *Staphylococcus aureus*. However, compound dispyrrole was found to have moderate antibacterial activity and dispyrrolopyridine A at concentration of MIC 8 $\mu\text{g}/\text{mL}$ was observed as an active efflux pump inhibitor against *Escherichia coli* (Wang et al. 2022a, b). Seven new angucyclinones scaffold molecules as kumemicinones A–G were identified from fermentation product *Actinomadura* sp. KD439 which have shown cytotoxicity against P388 murine leukaemia cells, with IC_{50} values ranging from 1.8 to 53 μM (Zhang et al. 2022). Pradimicin-IRD, a polycyclic antibiotic, was identified first from *Actinobacteria Amycolatopsis* sp. IRD-009. Pradimicin-IRD has shown potential antimicrobial activity at MIC 3.1 $\mu\text{g}/\text{mL}$ against *Streptococcus agalactiae*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*. Additionally, the same group reported cytotoxicity activity of the compound against HCT-116 colon carcinoma cells with IC_{50} 0.8 μM in and 2.7 μM in MM 200 melanoma cells (Bauermeister et al. 2019).

2,2'-bipyridine pharmacophore bearing compounds dipyrimicin A and B were isolated from actinomycete strain, *Amycolatopsis* sp. K16-0194 in which dipyrimicin A was observed to have stronger antimicrobial activity than the dipyrimicin B (Izuta et al. 2018). In 2018, Bunbamrung et al. upon prolific chemical profiling on species *Actinomadura* sp. BCC47066 identified many new and known anthrone derivatives, indole derivatives and flavonoid glycosides. The group reported compounds like (+)-oxanthromicins E, F and G, (\pm)-hemi-oxanthromicin D, azanthromicin A, adxanthromicin A2, 3-methoxy oxanthromicin, and (\pm)-oxanthromicin G, (\pm)-hemi-oxanthromicin A, demethyloxanthroquinone, oxanthroquinone, oxanthromicin, quercetin 3-glucoside, kaempferol 3-glucoside and indole-3-carboxylic acid from *Actinomadura* sp. BCC47066. The isolated all compounds were also bioevaluated for antimicrobial activity and cytotoxicity against both cancerous (KB, MCF-7, NCI-H187) and non-cancerous (Vero) cells (Bunbamrung et al. 2018) (Fig. 4b).

Table 2 Bioactive secondary metabolite produced by endophytes

S. no	Bioactive secondary metabolite	Class of compound	Fungal endophyte	Host plant	Biological activity	References
1	Aconitine	Alkaloid	<i>Cladosporium cladosporioides</i>	<i>Aconitum leucostomum</i>	Anti-inflammatory and anti-tumour activity	Yang et al. 2013
2	Apigenin	Flavones	<i>Dichotomopilus funicola</i>	<i>Cajanus cajan</i>	Antioxidant activity	Gu et al. 2018a, b
3	Artemisinin	Lactone	<i>Pseudonocardia</i> sp.	<i>Artemisia annua</i>	Antimalarial activity	Li et al. 2012
4	Baccatin	Alkaloid	<i>Diaporthe phaseolorum</i>	<i>Taxus wallichiana</i>	Anticancer activity	Zaiyou et al. 2013
5	Berberine	Alkaloid	<i>Alternaria</i> sp.	<i>Coptis chinensis</i>	Antidiabetic activity	Zhang et al. 2016
6	Camptothecin	Alkaloid	<i>Trichoderma atroviride</i>	<i>Camptotheca acuminata</i>	Anticancer activity	Pu et al. 2013
7	Chaetomugilin A	Azaphilones	<i>Chaetomium globosum</i>	<i>Ginkgo biloba</i>	Anticancer activity	Yasuhide et al. 2008
8	Chaetomugilin D	Azaphilones	<i>Chaetomium globosum</i>	<i>Ginkgo biloba</i>	Anticancer activity	Yasuhide et al. 2008
9	Citrinin	Benzopyrans	<i>Penicillium</i> sp.	<i>Gastrodia elata</i>	Anticancer activity	Li and Chen 2020
10	Curcumin	Phenols	<i>Ovatospora brasiliensis</i>	<i>Curcuma caesia</i>	Anti-ageing activity	Majeed et al. 2019
11	Ergoflavin	Phenols	PM0651480	<i>Mimosops elengi</i>	Anticancer activity	Deshmukh et al. 2009
12	Eugenol	Phenols	<i>Neopestalotiopsis</i> sp. and <i>Diaporthe</i> sp.	<i>Cinnamomum loureiroi</i>	Antimicrobial and antioxidant activity	Deshmukh et al. 2009
13	Huperzine A	Alkaloid	<i>Colletotrichum</i> sp.	<i>Huperzia serrata</i>	Alzheimer's disease	Sang et al. 2020
14	Luteolin	Flavonoids	<i>Phomopsis liquidambari</i>	<i>Bischofia polycarpa</i>	Antioxidant activity	Wang et al. 2015
15	Paclitaxel	Alkaloid	<i>Phoma medicaginis</i>	<i>Taxus wallichiana</i>	Anticancer activity	Zaiyou et al. 2017
16	Piperine	Alkaloid	<i>Colletotrichum gloeosporioides</i>	<i>Piper nigrum</i>	Antimicrobial and antioxidant activity	Chithra et al. 2014
17	Podophyllotoxin	Lignan	<i>Phialocephala fortinii</i>	<i>Podophyllum peltatum</i>	Anticancer activity	Uzma et al. 2018
18	Quercetin	Flavonoids	<i>Psathyrella candolleana</i>	<i>Ginkgo biloba</i>	Anti-ageing activity	Pan et al. 2020
19	Resveratrol	Stilbenoid	<i>Arcopilus aureus</i>	<i>Vitis vinifera</i>	Antimicrobial and antioxidant activity	Dwivedi and Saxena 2018
20	Secalonic acid D	Alkaloid	<i>Blennoria</i> sp.	<i>Carpobrotus dulcis</i>	Antimicrobial activity	Zhang et al. 2009
21	Syringin	Phenols	Members of xylariaceae	<i>Syringa vulgaris</i>	Antidiabetic activity	Singh et al. 2021a, b
22	Torreyanic acid	Quinones	<i>Pestalotiopsis</i> sp.	<i>Clavarioides</i> sp.	Antimicrobial activity	Ding et al. 2017
23	Vanillin	Phenols	<i>Xylaria allantoides</i>	<i>Schinus terebinthifolius</i>	Antimicrobial activity	Dos Santos et al. 2021
24	Vinblastine	Alkaloid	<i>Alternaria</i> sp.	<i>Catharanthus roseus</i>	Anticancer activity	Uzma et al. 2018
25	Vincristine	Alkaloid	<i>Fusarium oxysporum</i>	<i>Catharanthus roseus</i>	Anticancer activity	Uzma et al. 2018
26	Withanolide A	Alkaloid	<i>Withania somnifera</i>	<i>Aspergillus terreus</i>	Anticancer activity	Kushwaha et al. 2019
27	Hypericin	Anthraquinone	<i>Acremonium sclerotigenum</i>	<i>Hypericum</i> sp.	Antidepressive, antineoplastic activity	Kubin et al. 2005
S. no	Bioactive secondary metabolite	Class of compound	Bacterial/Actinomycetes endophyte	Host plant	Biological activity	References
28	6-Prenylindole	Alkaloids	<i>Streptomyces</i> sp.	<i>Allium tuberosum</i>	Antifungal activity	Singh and Dubey 2018
29	1-Acetyl- β -carboline	Alkaloids	<i>Aeromicrobium ponti</i>	<i>Vochysia divergens</i>	Antibacterial activity	Gos et al. 2017
30	3-Acetonilydene-7-Prenylindolin-2-one	Alkaloids	<i>Streptomyces</i> sp.	<i>Glycine max</i>	Antifungal activity	Zhang et al. 2014

Table 2 (continued)

31	Vindoline	Alkaloids	<i>Microbacterium</i> sp.	<i>Catharanthus roseus</i>	Treating Hodgkin's disease and acute leukaemia	Anjum and Chandra 2019
32	Camptothecin	Alkaloids	<i>Kytococcus schroeter</i>	<i>Ephedra foliata</i>	Anticancer activity	Ghiasvand et al. 2020
33	Indole-3-acetic acid	Alkaloids	<i>Pseudomonas fluorescens</i>	<i>Atractylodes lancea</i>	PGPR activity	Ghiasvand et al. 2020
34	Berberine	Alkaloids	<i>Microbacterium</i> sp. and <i>Burkholderia</i> sp.	<i>Coptis teeta</i>	Anti-inflammatory, anti-tumour activity	Anjum and Chandra 2019
35	Cedarmycin A	Lactones	<i>Streptomyces</i> sp.	<i>Aucuba japonica</i>	Antifungal and antibacterial activities	Singh and Dubey 2018
36	Daunorubicin	Lactones	<i>Paenibacillus polymyxa</i>	<i>Ephedra foliata</i>	Anticancer activity	Gos et al. 2017
37	Hookerolide	Lactones	<i>Streptomyces</i> sp.	<i>Maytenus hookeri</i>	Antimicrobial activities	Singh and Dubey 2018
38	Trans cinnamic acid	Organic acids	<i>Nocardopsis</i> sp.	<i>Zingiber officinale</i>	Antimicrobial activity	Gos et al. 2017
39	phthalic acid	Organic acids	<i>Bacillus atrophaeus</i>	<i>Glycyrrhiza uralensis</i>	Antifungal and antibacterial activities	Singh and Dubey 2018
40	Benzoic acid	Organic acids	<i>Nocardopsis</i> sp.	<i>Zingiber officinale</i>	Antimicrobial activity	Gos et al. 2017
41	Halobacillin	Cyclopeptides	<i>Streptomyces</i> sp.	<i>Bruguiera gymnorrhiza</i>	Anti-HIV activity	Zhang et al. 2014
42	Ginsenoside Rg3	Saponins	<i>Burkholderia</i> sp.	<i>Panax ginseng</i>	Anticancer activity	Singh and Dubey 2018
43	Ginsenoside Rh2	Saponins	<i>Agrobacterium</i> sp.	<i>Panax ginseng</i>	Anticancer activity	Zhang et al. 2014

Application towards sustainable agriculture

According to the UN Food and Agriculture Organisation (FAO), farmers would need to produce 70% additional foods by 2050 to fulfil the worldwide demands of a population of 9 billion people. Nowadays, people are choosing natural-based fertilisers over chemical based as they are costly, non-eco-friendly and cause a harmful impact on environment. Microbial origin fertilisers, like endophytic fungi, endophytic bacteria, etc., can promote plant growth and health, disease resistance property, stress tolerance property, biocontrol agents and food security. Alongside, microbial origin fertilisers are economical, eco-friendly, effective and increase the abiotic and biotic stress tolerance. Plant-associated microbiomes are important for improving plant nutrition. Plant symbioses with AMF and *Rhizobium* bacteria have been intensively investigated in the molecular pathways driving nutrient acquisition (Mandal et al. 2010). Furthermore, non-symbiotic bacteria that support plant development can either enhance insoluble mineral bioavailability or enhance the root system framework of host plants, boosting the root's water and mineral exploration capability (Liu et al. 2020). The microbiome influences the functional properties of plants relating to nutrient uptake or conservation that separate exploitative (rapid-growing) from conservative (slow-growing) plant species (Pii et al. 2015). According to recent research, variations in rice varieties' nitrogen usage efficiency are attributed towards the need of more nitrogen cycled symbiotic bacteria in the root biome of *Oryza indica* variety as compared to the *Oryza japonica* (Qin et al. 2020; Zhang et al. 2019; Trivedi et al. 2020) (Fig. 2) (Table 1).

Role of endophytes in plant growth promotion

For ages, endophytes particularly bacteria, actinomycetes and fungi are considered indispensable microorganisms due to their ever-present relationship with miscellaneous plant species. Microbial endophytes are also endowed with inexhaustible proficiency for advancing the plant growth. Endophytes promote plant growth via two mechanisms referred to as direct plant growth promotion (DPGP) and indirect plant growth promotion (IPGP). In the DPGP mechanism, endophyte fungi and bacteria own the competency to perform enhancement of plant growth by production and regulation of phytohormone (indole-3-acetic acid, cytokines, gibberellins), improvement of antioxidant activity and augmentation of nutrient movement or procurement. Indole 3-acetic acid (IAA) is studied as the predominant and effective plant auxin as it is extensively generic and one of the eminent metabolites involved in plant development with regard to

supporting apical pre-eminence, improved photosynthesis, progression of roots, mechanism of cell division, nodule evolution and pigment production. Approximately 34% of endophytes such as *Rhizobium* sp. and *Enterobacter asburiae* have the potential to produce IAA. Another one of the influential and imperative phytohormone controlling seed propagation, stem induction, emanation of seed and flower maturation is gibberellins. Endophytes like *Acetobacter diazotrophicus* and *Herbaspirillum seropedicae* have been affirmed to synthesise gibberellins, eventually aids in plant growth (Rana et al. 2020), whereas the indirect plant growth promotion mechanism is performed by bacterial endophytes, prohibiting the pernicious response by certain pathogens and restraining abiotic stress.

The host plant and endophytes live in mutual symbiotic relationship, where the endophytes live as a host in the plant and help plant to survive against abiotic and biotic stress. For an instance, endophytes produce enzymes such as dehydrogenase, cellulase, chitinase and lipase required for degradation of microbial cell wall to combat the biotic stress in plants (Slama et al. 2021). Endophytic *Streptomyces* sp. is an *Actinobacteria*, existing as a rhizospheric microbial community and is considered potent plant tissue coloniser having the ability to enhance plant growth. *Streptomyces* function as a nutrient augments, soil fertility enhancer, IAA producer, gibberellins synthesiser and siderophore producer. *Streptomyces* has been known to increase the seed germination potential due to IAA synthesis (Vurukonda et al. 2021). In a literature study, increased yield and improved plant growth in case of cucumber were accomplished due to the endophytic *Streptomyces spiralis* (Jog et al. 2012). The other mechanism through which endophytes contribute to plant growth is siderophore production. Endophytes secrete siderophores which are adept at chelating iron. Siderophores facilitate the improvement of iron deficient plants and aids in nitrogen fixation as for the synthesis and working of nitrogenase, diazotrophic microbes demand ferrous ion as well as molybdenum factor. In bacterial membrane, iron (II) oxide is converted to iron (III) oxide that is brought inside the cell by endophytes via gating system. As the siderophores attached to metal, soluble metal's concentration also rises. Plants use numerous techniques for the absorption of iron from siderophore producing endophytes such as the chelation of Fe is involved in the exchange of ligands or the direct iron-siderophore absorption (Mahanty et al. 2017). *Streptomyces acidiscabies* E13 is an eminent hydroxamate siderophore producing endophyte, within nickel stress situation which is known to improve the *Vigna unguiculata* L. (cowpea) growth (Sharma et al. 2020). In a literature study, *Pseudomonas* GRP3 endophytic producer of siderophore was examined for Fe nutrition on *Vigna radiata*. Consequently, after one and a half month, a decreased in chlorotic aspect and iron content were

observed. Compared to control, an increase in concentration of chlorophyll a and b content were reported in *P. Grp3* inoculated plant (Lingua et al. 2020). Consequently, such studies highlight the application of endophytes as efficient plant growth promoters.

Endophytes as biocontrol agent

One of the arising concerns in the field of agronomics is the piecemeal downturn in productivity of agricultural produce due to biotic and abiotic stress. The serious determinant to strengthen arboriculture progress exists in managing plant diseases caused by numerous bacteria, viruses and fungi ultimately leading to critical crop loss. To ensure continuous dynamic agricultural structure and control of plant disease, fungicides, insecticides, pesticides and herbicides perform powerful role. But the extensive use of agrochemicals results in detrimental effects on functioning of environment, agricultural economic growth and ultimately on humans. The persistent and superior economic development of agricultural system can be attained by the eradication of chemical pesticides to have a positive influence on the ecosystem. Currently, the application of endophytes as biocontrol agents has attracted pivotal consideration as an alternative option for chemical fertilisers. Endophytes act as proficient biocontrol agents by altering association with pathogens and pests. In comparison to non-endophytes, *Epichloe typhina* was identified as the first fungal endophyte of *Phleum pretense* (timothy grass) having the competency to battle against *Cladosporium* (De Silva et al. 2019). Fungal endophyte, *Acremonium alternatum*, has been reported to restrict harm caused in beans by *Plutella xylostella* and is known to induce resistance against powdery mildew pathogen *Leveillula taurica* (Ek-Ramos et al. 2013). Endophytes have been recorded to synthesise numerous natural compounds such as terpenoids and alkaloids, which function as biocontrol agents, antibiotics and immune suppressors, and exhibit anti-cancerous properties (Rana et al. 2020). Endophytes have also been documented to generate secondary metabolites like taxol, camptothecin, podophyllotoxin and deoxypodophyllotoxin against pathogens or pests with promising biological activity. Deoxypodophyllotoxin is synthesised by *Aspergillus fumigates* endophyte in *Juniperus communis* which is well known to work against pathogenic microbes (De Silva et al. 2019). Such reported studies demonstrate the ability of endophytes to act as potential biocontrol agents.

Table 3 Gene transfer (biosynthetic secondary metabolite clusters) from endophyte to plant as well as plant to endophytes

S. no	Endophytes	Host plant	Gene transfer	Inference	Reference
Endophyte to plant					
1	<i>Epichloe</i> (syn. <i>Neotyphodium</i>)	Perennial Ryegrass	β -1,6-glucanase gene	Fungal cell wall degradation	Shinozuka et al. 2017
2	<i>Pseudomonas Putida</i> W619-TCE	Poplar	TCE degrading enzyme	Degradation of TCE soil contamination	Weyens et al. 2015
Plant to endophyte					
1	<i>Cladosporium cladosporioides</i> MD213	<i>Taxus brevifolia</i>	Taxadiene synthase (<i>tax</i>), baccatin amino phenylpropanoyl transferase (<i>bapt</i>)	Taxol synthesis	Zhang et al. 2009
2	<i>Fusarium solani</i>	<i>Camptotheca acuminata</i>	<i>G10H</i> , <i>SLS</i> , <i>STR</i>	Camptothecin	Kusari et al. 2011
3	<i>Agrobacterium tumefaciens</i>	<i>Pteris vittata</i> L.	<i>arsB/ACR3(2)</i> genes	Alleviating arsenic (As) contamination	Guet et al. 2018a, b
4	<i>Fusarium proliferatum</i>	<i>Orchid root</i>	GA biosynthetic gene P450-4	Gibberlic acid synthesis	Kumara et al. 2014
5	<i>Cladosporium cladosporioides</i>	<i>Aconitium leucostomum</i>	Methyl and acyl transferases	Aconitine	Singh et al. 2021a, b
6	<i>Biscogniauxia cylindrospora</i>	<i>Acanthopanax senticosus</i>	Phenylalanine ammonia-lyase (PAL) and cinnamate 4-hydroxylase (C4H)	Isofraxidin	Srinivasa et al. 2022
7	<i>Penicillium polonicum</i> hy4 and <i>Colletotrichum gloeosporioides</i> Cg01	<i>Hydrangea serrata</i>	Lysine decarboxylase (LDC), copper amine oxidase (CAO), polyketides synthases (PKS)	Huperzine A	Kang et al. 2019
8	Endophytic fungi HL-Y-3	<i>Coptis chinensis</i>	<i>CYP80B2</i> , <i>4'OMT</i> and <i>CYP719A1</i>	Berberine	Zhang et al. 2016
9	<i>Arcopilus aureus</i>	<i>Vitis vinifera</i>	Resveratrol O-methyltransferase	Pterostilbenes	Dwibedi and Saxena 2018; 2022
10	<i>Arcopilus aureus</i>	<i>Vitis vinifera</i>	Stilbene Synthase (STS), 4-coumarate CoA-ligase (<i>4CL</i>)	Resveratrol	Dwibedi and Saxena 2018; 2022
11	<i>Arcopilus aureus</i>	<i>Vitis vinifera</i>	Stilbene Synthase (STS), 4-coumarate CoA-ligase (<i>4CL</i>)	Piceatannol	Dwibedi and Saxena 2018; 2022
12	<i>Arcopilus aureus</i>	<i>Vitis vinifera</i>	Stilbene Synthase (STS), 4-coumarate CoA-ligase (<i>4CL</i>)	Piceid	Dwibedi and Saxena 2018; 2022
13	Endophytes of <i>Morus alba</i>	<i>Morus alba</i>	Stilbene Synthase (STS), 4-coumarate CoA-ligase (<i>4CL</i>), Phenylalanine ammonia-lyase (PAL)	Mulbroside	Valletta et al. 2021
14	<i>Periconia</i> sp., <i>C. gloeosporioides</i>	<i>Piper nigrum</i>	Piperoyl-CoA ligase, Piperine Synthase	Piperine	Singh et al. 2021a, b

Genome mining of endophytes for sustainable agriculture and food security

The field of agronomics is confronting different problems to generate enough quality edible material in a sustainable demeanour with diminishing food resources and expanded worldwide populace. The production as well as yield is largely affected by the overabundance of biotic and abiotic stress due to various pathogens. However, the common suggestion to control such rising issues is the utilisation of chemical pesticides and insecticides which further boost accumulation of toxic components within ecosystem. Plant-associated microbes like endophytes prove to be beneficial to agriculture by generating profit for plants in terms of producing phytohormone, promoting plant growth, as bio-control agents and providing resistance to host plant (Vurukonda et al. 2018). In a literature study, Eida et al. conducted the genome sequencing of a plant growth promoting endophyte, *Paenibacillus* sp. JZ16, which belongs to a halophile *Zygothymum simplex*. Nine secondary metabolite regions were identified using anti-SMASH analysis, two clusters were similar to ectoine and paenibactin biosynthesis. Ectoine is a consistent solute eminent in halophiles while paenibactin is well-known catecholate kind of siderophore. *Paenibacillus* sp. JZ16 was documented with *ectABC* genes being converted into *ectD* (hydroxyectoine) which further encodes for ectoine biosynthesis consequently providing salt stress and osmotic tolerance to *Paenibacillus* sp. JZ16 (Eida et al. 2020). Chlebek, Pinski et al. explored the remarkable perspective of endophyte *Pseudomonas fluorescens* BRZ63 of *Brassica napus* (oilseed) plant as a biocontrol agent against fungal pathogens including *Sclerotinia sclerotiorum* K2291, *Rhizoctonia solani* W70, *Fusarium avenaceum* and *Colletotrichum dematium* K. The genes that were involved in the coding of two different lytic enzymes were *nagA* for N-acetylglucosamine-6-phosphate deacetylase and *bgIX* for beta glucosidase. *P. fluorescens* BRZ63 demonstrates biocontrol activity by encoding genes including *phzF*, *trdG*, *ubiC*, *pys2* and *prlC* gene. For the competitive iron acquisition, *P. fluorescens* BRZ63 proves to be immensely efficacious due to the presence of Ton B dependent receptor genes. The other eminent genes include *trpABCDE* and *iscU* for synthesis of tryptophan and nitrogen fixation respectively (Chlebek et al. 2020). Such studies demonstrate greater perspective of endophyte's interaction with host plant and endophytic genes that contributes to sustainable agriculture. Intergeneric genetic exchange between the endophytes and their host leads to a symbiotic relationship between them. This gene transfer allows endophytes to take up host genome fragments. Endophytes are widely

screened for genes responsible for host-derived phytochemical production in endophytes, while other studies reveal that genes encoding biosynthetic pathways responsible for secondary metabolite production in endophytes which is not homologous to the plant genes (Table 3).

Multi-omics approaches to deciphering endophytic adaptation for sustainable agriculture and food security

Endophytes are considered one of the effective sources for the production of secondary metabolites, which have various applications in industries like agriculture, food and healthcare sectors. Endophytes also enable the host plants to survive in response to abiotic and biotic stress and research is still going on to search other beneficial aspects of endophytes. Omics can be a routeway technology for better understanding between the host and endophytes relationship and can be explored for the applications such as bioremediation, plant growth promotion and biocontrol. The demand of the era is to understand the function of mutualistic relationship of endophytes with their respective host plant. Methods like microarray, genome sequencing, next-generation sequencing (NGS), comparative genomics, metatranscriptomics and metagenomics are few of tools from the pool of omics technology used to explore genomics and host-endophyte relationship. The molecular techniques are the successful tools for identification and exploring the host-endophytes relationship. For instance, NGS evaluates the RNA or DNA sequences with immediate output in an effective manner (Gupta et al. 2021). With the practice of multi-omics approaches, the profound mechanism behind the host and endophytes can be studied well. The information-guided microbial cultivation technology is a new feasible, user-friendly technique to monitor and control the growth of microbial culture so as to exchange or enhance the production of secondary metabolites which can increase the interest in industrial biotechnology. Endophytes are not only diverse but also have an abundance of transcriptional regulators. There is a subset of families that are responsible for metabolic adaptation, bacterial virulence and quorum sensing were identified such as the Ic1R family, Crp family, AraC family and LysR family. For agriculture sustainability, major protein domains responsible for the production of GGDEF were analysed. In the symbiotic association of rice and endophytes, higher encoding of phosphodiesterase A genes was because of degradation of HID-GYP and EAL. Reduction in the levels of c-di-GMP by PDEA was responsible for motility of bacteria whereas excessive amounts

were beneficial as they lower infections and enhance the formation of biofilm (Adeleke and Babalola 2022). In *Aloe vera* plants, the endophytic strains that are culturable or unculturable were revealed by analysis using NGS. The microbial range and the colonisation pattern of endophytes were estimated. This omics approach enables to analyse the composition and diversity among species. During this study, high throughput techniques of NGS were applied to metagenomics and metaproteomic study. In *Aloe vera* plants and endophytic bacteria association, its V3-V4 regions were assessed by PCR amplification and then by approaching Illuminametagenomics 5,299,102 reads were generated from the sample. This analysis revealed that *Actinobacteria*, *Proteobacteria*, *Bacteroidetes* and *Firmicutes* were predominantly present (Dubey et al. 2020). Metabolomics approach was carried out to study the resistance factor of nematodes in tomato (*Solanum lycopersicum*). In resistant plants, interaction of nematodes and tomato plant some metabolites were observed includes primary metabolites as α - and β -glucose and secondary compound as caffeic acid. Caffeic acids are found in higher concentrations in aromatic region. The precursor of essential compounds responsible to resist against biotic stress is synthesised by such types of sugar compounds. These compounds play a vital role in triggering signal pathways and enhancing resistance against pathogens (Pentimone et al. 2020). Proteogenomics was used to carry out study of identification of traits which are exclusive in endophytic bacteria colonising *Arabidopsis* host plants leaves. For transcriptome analysis, cDNA microarrays such as Nchip TM microarray and Endochip TM microarrays were used to describe the potential of *Epichloe* and *Neotyphodium* endophytes in *Arabidopsis*. Study revealed that due to endophytes, the Et responsive genes were downregulated and genes related to production of plant hormones and formation of nodules were upregulated (Wang et al. 2022a, b). Another study was carried out utilising symbiosis chip-based tools named as Affymetrix Gene to study in *Medicago truncatula* host plant and it is the synchronise differentiation with endophytic strain *Sinorhizobium meliloti* during the formation of nodules. The expression of key regulatory proteins such as NodD3, RpoN and NodD1 were responsible for the modification and rich amounts of luteolin, a host plant signalling molecule was found to be expressed. In *Saccharum officinarum*, quantitative mass spectroscopy-based proteomics analysis was carried out, which were colonised *Gluconacetobacter diazotrophicus* to study its molecular aspects. In this study, analysis of more than four hundred proteins was carried out and among them, seventy-eight of proteins were identified for expressing differentially (Waghunde et al. 2017).

Ofek-Lalzar et al. (2016) studied the fungal diversity of endophytes isolated from stem and seeds samples of *Triticum dicoccoides* and *Aegilops sharonensis*. The classification at

97% sequence similarity resulted in 67 operational taxonomic units (OTUs) evenly dispersed among diverse plant species. Endophytes are found to be a part of various plant species. More recently, the metabolomic methodologies were established compared to transcriptomics, metagenomics and proteomics (Chlebek et al. 2020). The changes in the habitat of endophytes or host plant species can be attributed to the metabolic profile of the system. Alteration in the environmental conditions directly reflects the metabolic profile of biological systems (Carrell et al. 2022). The end product of the central dogma results in the synthesis of biochemical metabolites within the microbes. The biotic and abiotic stress can alter the expression of microbial metabolites that help them survive and tolerate adverse conditions (Rinschen et al. 2019; Lakrisenko and Weindl 2021).

Molecules like alkaloids, amino acids, carbohydrates, flavonoids, minerals, nucleic acids, organic acids, peptides, polyphenols, vitamins, etc. included in metabolome are synthesised by the endophytic cell. The majority of them have a positive impact to accommodate in adverse conditions and also promote the host plant's health (Balestrini et al. 2021). These molecules need to be identified and more concern should be given to find applications to improve health. The techniques in advancement to identify and analysed are being developed to explore more information about the molecule structure and interaction with other molecules. Techniques such as Fourier transform infrared (FT-IR), ultra-high-resolution Fourier transform ion cyclotron resonance-MS, gas chromatography-mass spectrometry (GC-MS) and nuclear magnetic resonance (NMR) spectrometry are more focused to analyse and identify the molecule of interest (Misra 2021).

If we talk about the role of molecules produced under stress conditions by the endophytic microbes, it is important to identify and isolate the molecule and study it at the molecular level. Techniques like metabolite fingerprinting can improve the finding and result analysis in total compositions of metabolites. Additionally, the quality of spectra can be improved with the application of nanoflow-direct infusion QTOF mass spectrometry (Mishra et al. 2022). Mass analyzers like time-of-flight mass spectrometry (TOF-MS), Orbitrap Mass Spectrometer (Orbitrap-MS) and Fourier transform ion cyclotron resonance-mass spectrometry (FTICR-MS) that are mostly applied can be used to determine the mass of cell and compounds. Identification of various metabolites can be done with accuracy through techniques like HPLC, GC and capillary electrophoresis (Ghaste et al. 2016).

Proteomics is the large-scale protein analysis; the analysis is based on the fact that final protein product is inherited as complex protein through a series of process involved in protein modification involved post-translation modifications. The proteomics rubrics include the study of protein function protein, protein modifications, protein interaction studies and protein localization. Proteomics approach is used to

evaluate the relationship between the host and endophytes in terms of signalling process, colonisation and components of the factors, etc. (Raghu et al. 2021). Another field to explore is Proteogenomics, an interface of proteomics and genomics. This approach is applied to find out novel peptides by retrieving the information from the protein database generated through proteomic and genomics databases. Exploring the proteomics data derived through mass spectrometry-based analysis. Another example is Riboproteomics (integrated profiling of RNA–protein and protein–protein interactions), a novel approach to study the function of RNA-binding proteins, which helps to define symbiotic RNA–protein profiles and protein–protein networks (Cozzolino et al. 2021). Techniques such as multi-dimensional protein identification technology (MudPIT), In vitro isotopic labelling method used for quantitative proteomics (ICATs), tandem mass tag (TMTs) and isobaric tags for relative and absolute quantitation (iTRAQ) used as “second generation” for the investigation of global or cellular proteomes of plants exposed to abiotic stress (Chandramouli and Qian 2009; Bai et al. 2021) (Fig. 5).

Conclusions

Microbial products such as bio-fertilisers, bio-stimulants and bio-control agents have been used more often in the past few years, although their performance has been uneven. Major processes controlling the assembly of plant-associated microbiota have been revealed by genome-wide, metagenome-wide association studies and connections between specific microbial taxa and genes and plant colonisation, physiology and fitness variables. A significant portion of the variation in community assembly and microbiome consequences for plant fitness is still unexplained. To close these gaps, larger-scale longitudinal research will be needed to establish baselines for plant-associated microbiomes that explicitly account for temporal dynamics and age of host. While much progress has been made in recent years in understanding multipartite (for example, plant–animal–soil or plant–environment–soil) interactions in the phytobiome, little is known about the microbiome’s functional characteristics. There is, however, no consensus on acceptable microbiological endpoints (what defines a “healthy” microbiome). NGS and experimental techniques, we hope, will be able to tackle certain methodological and technological challenges in the future. Data translation to phenotypic relationships, experimental modelling with co-cultivation or gnotobiotic techniques and multi scale computational simulations are only a few examples. These integrative methodologies will bring together knowledge, skills and processes from a wide range of disciplines in science, engineering and other fields. The ability to create vast microbial consortia with

predictable behaviour and powerful repercussions will be aided by a greater understanding of the dynamic interactions between plants, microbiomes and the environment. In the future, endophytic microbes may prove to be more effective bio-inoculants and bio-controlling agents for plant growth and development of plants under several climatic stressors. This might be utilised to build crop-specific endophytic consortiums for even more sustainable agriculture.

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Author contribution VD: conceptualization, investigation, original draft and review and editing. SKR: data creation, software, formal analysis and review and editing. RK: investigation, formal analysis and review and editing. MJ: investigation, formal analysis and review and editing. GK: investigation and formal analysis. SJK: conceptualization, methodology, validation, project administration and review and editing.

Declarations

Ethics approval This article does not contain any studies with human participants or animals performed by any of the authors.

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