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CHAPTER 7

Microbiota of Medicinal Plants: Implications in Health

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Abstract

Recent studies in Medicinal Plant Research have highlighted that a substantial proportion of phytotherapeutic compounds is generated by their related microbes or through reaction with their host. Medicinal plants generate unique and structurally varied bioactive secondary metabolites because of their own distinct microbiome. The high specificity of related microorganisms is probably a result of these metabolites. This review specifically examines the microbiota of Medicinal Plants and their role in the production of plant antimicrobial compounds, which are essential for health and therapeutic properties, making them valuable resources for application in biotechnology and medicine.

Keywords: Medicinal Plants, Bioactive Compound, Microbiota, Health

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Introduction

The planet is home to approximately 35,000 species of vascular plants with potential medicinal applications. Furthermore, according to reports, 80% or more of the global population uses conventional herbal treatments, and plants provide 25% of the biologically active substances found in different medications (Miranda 2021). Medicinal herbs contain various chemical compounds with diverse structures and functions that demonstrate significant biological activities. Antioxidant, antiviral, antimicrobial, enzyme inhibitory and cancer preventing properties are among the many positive attributes linked to these compounds. They also have anti-aging, anti-inflammatory, antihypertensive, anticoagulant and neuroprotective properties (Lesellier et al 2021). Given the rise of bacteria resistant to antibiotics, the exploration of new bioactive substances is increasingly important. Medicinal plants contribute to 25-50% of the pharmaceuticals utilized in modern healthcare (Sian et al 2020). Globally, there is a search for new bioactive compounds from both familiar and rare plants (Fettach et al., 2019). Bioactive substances can be found in the stems, roots, leaves, flowers, fruits and seeds of medicinal plant species. (Knez Hrnčič et al. 2020). According to studies, bioactive compounds obtained from plants provide protective and health-promoting effects in humans and animals. Pharmaceutical sectors and end users find them desirable due to their reputation as natural, less harmful, with fewer adverse effects than chemical-based drugs.

Medicinal plant research is undergoing a shift in focus due to the realization that many phytotherapeutic compounds are created by microbes that are associated with the plants or through their interaction with the host (Zhou et al. 2016). When plants are used in therapeutic application, they are intricate systems affected by various factors such as the kind of plant, biochemical profiles, the specific part of the plant used, storage conditions, humidity, sunlight exposure, harvesting timing, and geographic location. Recent studies on the relationship between medicinal plants and endophytes have revolutionized our comprehension of plant biology, opening up unexpected and significant possibilities for practical application. Researchers are investigating the microbiota's capacity to impact the production of phytoconstituents like terpenes, polyphenols, and alkamides, as well as to create new molecules with antibiotic properties (Castronovo et al 2021). The current investigation deals with overview of microbiota found in medicinal plants and their interaction with the host to produce important phytochemicals with role in biocontrol, enhancing the health of host plant and implication in plant therapeutic properties. The role of the microbiota in contributing to plant therapeutic properties indicate its future prospect to be utilised as resource for the pharmaceutical and biotechnological industries.

Diversity of Microbiota in Medicinal Plants

Plants with therapeutic properties have a unique microbiome because of their structurally and chemically distinct biologically active secondary metabolites. This microbiome is probably what accounts for their highly characteristic microorganisms (Qi et al., 2012). A number of secondary metabolites secreted by medicinal plant roots affect the variety of microbial communities in the rhizosphere. Among the most prevalent bacteria found in medicinal plants are *Microbacterium*, *Bacillus, Burkholderia Rhizobium, Serratia, Pseudomonas, Beijerinckia, Azotobacter* and *Enterobacter*. Inorganic phosphorus is solubilized in the rhizospheres of medicinal plants by the Actinobacteria present in the rhizosphere that release small organic solutes (Jabborova et al 2024). The microbiome comprises of various microbial populations located in the endosphere, shoots, and roots (Beneduzi et al 2012). Studies indicate that the rhizosphere of plants can serve as a source of beneficial microorganisms for plant health (Weller DM 2002; Berendsen R.L 2012). Knowing the ecology of bacteria associated with plants can offer insights into how microbial communities adapt to the physical and chemical environment of the rhizosphere. It has been noted that the rhizospheres of medicinal plants such as common marigold (*Calendula officinalis*), sweet false chamomile (*Matricaria chamomilla*), and *Solanum distichum* hold a significant number of antagonistic bacteria (Koberl M. 2013). Endophytic fungi found in *Azadirachta* can serve as a source of bioactive antimicrobial and insecticidal compounds, such as azadirachtins and tetranortriterpenoids. Researchers (Kaur et al 2013) have identified four species of endophytic fungi (*Trichoderma sp., Colletotrichum sp., Curvularia sp*., and *Chaetomium sp*.) and *Alternaria alternata* isolated from *Azadirachta indica* A. Juss leaves. In Varanasi, India, *Chloridium sp*. was isolated from the roots of *A. indica* A. Juss, with the fungus producing antibacterial functionalized javanicin, potentially protecting the host from pathogens (Kharwar et al 2009). Verma et al. (2011) have reported the isolation of 167 endophytic fungi from the roots at a rate of 68.0%, with 29 identified taxa; mycelia sterilia accounted for 11.06%, coelomycetes 7.25%, and hyphomycetes the highest proportion at 81.69%. They have also documented species like *Chaetomium globosum, Chloridium, Scytalidium, Nigrospora*, and *Verticillium* exclusively from the roots. Novel phosphate solubilizing endophytic fungus, *Eupenicillium parvum,* have also been characterized (Kusari et al. 2014)

Interaction of Medicinal Plants and Microbiota: Role in Production of Potential Biocontrol Compounds

Rhizospheric microorganisms offer advantages to plants through diverse mechanisms. Enhanced nutrient uptake or hormonal stimulation directly contributes to plant growth, while the suppression of phytopathogens can indirectly influence it (Lugtenberg and Kamilova, 2009; Berg, 2009). Microbes that stimulate plant growth are better known as phytostimulators. An example is the production of the phytohormone auxin by fluorescent pseudomonads (Khare and Arora, 2010). Plant growth is encouraged by rhizobacteria such as *Burkholderia cepacia, Bacillus subtilis, Staphylococcus epidermidis* that release volatile organic compounds (VOCs) (Effmert et al., 2012; Bitas et al., 2013).

Phytopathogens can be controlled biologically to indirectly increase plant growth. Antibiotics, toxins, volatile organic compounds (VOCs), biosurfactants, and enzymes that degrade extracellular cell walls can all stop the growth of pathogens. However, competition for nutrients and minerals, or sites of colonization, as well as the breakdown of disease-causing factors like toxins, can also lead to microbial antagonistic effects (Berg, 2009). Induced systemic resistance (ISR), which is brought on by particular benign root associated bacteria, is another possible tactic to lessen the effect of disease-causing microorganisms. Flagella, lipopolysaccharides, siderophores, volatile organic compounds, and some other bacterial components are considered to activate the signaling pathway for ISR mediated by non-pathogenic rhizobacteria (Lugtenberg and Kamilova, 2009).

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In the realm of sustainable agriculture, there has been growing interest in utilizing biological methods to combat diseases and harnessing microorganisms to support development of plants, presenting sustainable alternatives to chemical fertilizers and pesticides (Weller, 2007). Although a number of microbial inoculants have already been successfully introduced to the market (Berg, 2009, 2013), medicinal plants, which are becoming more vulnerable to different soil-borne plant diseases, do not yet have a specific biological control strategy. The microbiomes linked to medicinal plants, which exhibit exceptional metabolic activity, have the potential to produce new biocontrol agents even though these plants require unique biocontrol agents.

Medicinal Plant Microbiota and Human Health

The presence of beneficial microorganisms and their chemical by-products in medicinal plants is often linked to their ability to combat human pathogens (Mousa and Raizada, 2013). Given the global challenge of drug resistance, it is essential to identify and develop new therapeutic compounds from natural sources (Costelloe et al., 2010). Around 80% of endophytic fungi generate bioactive substances with herbicidal, antibacterial and antifungal properties (Schulz et al., 2002). As a result, fungal endophytes have emerged as a promising alternative for the development of novel antimicrobial drugs. Several medicinal plants including *Skimmia arborescens* Anders., *Mallotus yunnanensis* Pax et. Hoffm., *Garcinia morella* Desr., *Schima sinensis* (Hemsl. et. Wils) Airy-Shaw., *Evodia daneillii* (Benn) Hemsl., *Brandisia hancei* Hook. f. and *Meliosma squamulata* Hance. demonstrated significant effectiveness against clinical pathogens such as *Staphylococcus aureus, Pseudomonas aeruginosa, Candida albicans* and *Escherichia coli* which aligns with their conventional application for the treatment of skin as well as other infections (Zuo et al., 2012). Bacterial pathogens *Staphylococcus aureus* and *Bacillus cereus* are controlled by plants *Cinnamomum mercadoi, Sceletium tortuosum* L. (Kougoed), *Indigofera sulfruticosa*. Miller, due to the presence of endophytes *Nigrospora sphaerica URM 6060 Fusarium oxysporum, Pestalotiopsis maculans URM 6061.* The endophytic fungi *Phomopsis spp.* in the host plant *Garcinia sp.* is effective against the bacterial pathogen Mycobacterium tuberculosis. The target bacteria S. *aureus, B. cereus, P. aeruginosa* are controlled by *Mikania cordata* due to the endophytic fungi *F. equiseti, Phoma medicagnis* (Chandra et al 2024)

The Mexican medicinal plants have demonstrated antimicrobial properties and are effective against multi-drug-resistant pathogenic microbes of human (Jacobo-Salcedo Mdel et al., 2011).

Endophytic fungi contain different substances of biological activity like the alkaloids, steroids, terpenes, and polyphenolics, which are found to have antifungal, antibacterial, antioxidant, anticancer and antiviral properties (Gupta et al., 2020).

Researchers worldwide are investigating novel plant-derived compounds with potential anticancer properties, as some have the capacity to regulate cancerous cells.

Curvularia verruculosa and *Chaetomium nigricolor* from the leaves of *Catharanthus roseus* have anticancer property against He La Cells and MCF 7. The fungal endophytes *Phomopsis glabrae, Fusarium oxysporum, Alternaria sp.,* and *Aspergillus fumigates* from the leaves of *Pongamia pinnata,* *Eremophila maculate and Monardo citriodora* are effective against bladder cancer BXF 1218, MOLT4, PreB697 cancerous cell line and HCT-116 (colorectal carcinoma), A549 (lung cancer cell line), PC-3 (prostate cancer cell line) and MCF-7 (breast cancer cell line). Similarly, the stems of *Lophocereus marginatus* and *Ficus carica* also harbour the fungi *Lophocereus marginatus* and *Aspergillus neoniger* that have been found to have anticancer property against human breast cancer (MCF-7), human colorectal adenocarcinoma (HT- 29), K-562 and HUVEC cell lines. The leaves and fruit of *Morinda citrifolia* are effective against PC-3 (prostate cancer line), LU-1 (lung cancer line) and MCF-7 (breast cancer line) due to the endophytic fungi *Xylaria sp, Stemphylium solani,* and *Leptosphaerulina australis* (Chandra et al 2024).

The interactions of endophytic fungi, which are a reservoir of bioactive compounds, can be manipulated to develop new and potentially effective chemotherapeutic agents. Camptothecin from *Camptotheca acuminata*, Vinca alkaloids like the Vinblastine (VBL), vinorelbine (VRL) and vincristine (VCR), podophyllotoxin from *Podophyllum peltatum*, and taxol from *Taxus brevifolia* are among the anticancer drugs that have been clinically evaluated. Adhikari et al. (2023) documented the use of organic anticancer drugs derived from endophytic fungi. The naturally occurring bioactive compounds of endophytes may provide a new source for the evolution of anticancer drugs (Xie and Zhou, 2017; Uzma et al., 2018). Interest in endophytes as potential sources of advanced anticancer drugs grew after the discovery that paclitaxel originates from an endophytic fungus. Researchers have explored the anticancer potential of endophytic fungi isolated from various plants (Zaferanloo et al., 2018; Dhayanithy et al., 2019). Human cancer cell lines MCF-7 (breast), LU-1 (lung) and PC-3 (prostate) were found to be inhibited in their growth by *Leptosphaerulina australis, Stemphylium solani* and *Xylaria sp.* isolated from the leaves of *Morinda citrifolia* (Wu et al., 2015). According to Dhankhar and Yadav (2013), solvents derived from the endophytic fungi *Aspergillus sp.* JPY2, *Phoma sp.* and *Aspergillus sp.* JPY1 isolated from *Salvadora oleoides* have shown antidiabetic effects in rats with diabetes caused by alloxan. In many tropical and subtropical regions, malaria is the primary cause of death and morbidity and is one of the most prevalent infectious diseases. According to Ujam et al. (2022), fungal endophytes that were separated from *Azadirachta indica's* leaves and stem demonstrated antiplasmodial activity against *P. falciparum*.

The presence of alkaloids in *Papaver somniferum, Withania somnifera* and *Catharanthus roseus,* has demonstrated that the production of bioactive compounds can be enhanced by bacteria. This enhancement can occur either through direct modulation of expression of biosynthetic genes or indirectly by boosting plant biomass and overall health, for example, through activities such as indole acetic acid (IAA) production, nitrogen fixation and phosphate solubilization (Pandey et al 2016; Pandey et al 2018; Tiwari et al 2013).

Free radicals are associated with various diseases, including diabetes, asthma, cystic fibrosis as well as neurological disorders such as atherosclerosis, Alzheimer's disease, Parkinson's disease, epilepsy, autoimmunity disorders, Huntington disease, aging, autoimmunity disorders, cancer, rheumatoid arthritis, cardiovascular disease and cataracts. The unpaired electrons in free radicals cause chain reactions during oxidation reduction reactions, leading to these diseases. Antioxidants can effectively neutralize these naturally occurring or supplemented free radicals in the body (Prasad et al. 2015).

Chyawan prash, a powerful antioxidant formula (Parle and Bansal 2019; Balkrishna et al., 2021), consists of around 50 medicinal herbs and has been traditionally used in India for many years to treat or avert a number of health problems (Balkrishna et al., 2021). Numerous herbs that make up Chyawanprash have been shown to contain one or more endophytic organisms (Wang et al., 2018; Kouipou et al., 2019; Ullah et al., 2019; Su et al., 2021; Stranska et al., 2022). Traditional formulations containing endophytes have been demonstrated to possess antioxidant properties.

Future Prospects of Medicinal Plant Microbiota

The vegetative and reproductive parts of medicinal plants such as *A. vera, Emblica officinalis, O. basilicum, C. roseus*, *Morinda tinctoria, Justicia adhatoda* and *A. indica* contain reducing agents that are utilized to create nanoparticles (Thirumagal et al 2020). It has been noted that bacterial endophytes can also be responsible for the production of nanoparticles in this context (Sunkar and Nachiyar 2012). Antimicrobial research should extensively investigate nanoparticles capable of causing damage to the membranes and biofilms of Multiple Drug Resistant (MDR) bacteria (Christina et al 2013; Singh et al 2017). Biologically derived metal nanoparticles are considered to be safer and more compatible with living organisms compared to those produced using traditional chemical methods. For instance, creating silver nanoparticles with plant extracts is a productive and economical technique with a variety of biomedical uses (Bose and Chatterjee 2015). Endophytic strains of *Bacillus sp*. and the fungi *Penicillium sp*., isolated from medicinal plants such as *Adhatoda beddomei,, Garcinia xanthochymus* and *Curcuma longa* were able to produce silver nanoparticles (AgNPs) that exhibited antibacterial activity against *P. aeruginosa, E. coli, S. aureus, K. pneumoniae* and *S. enterica* (Singh et al 2017; Sunkar and Nachiyar 2012). Furthermore, AgNPs produced using the extract of *Pantoea ananatis*, an endophytic bacterium, displayed potent antimicrobial action against *Candida albicans* and *B. cereus* which are unable to be inhibited by traditional antibiotics. Therefore, the microbial community linked to therapeutic plants has significant potential in the fight against emerging MDR bacteria.

Conclusion

In summary, it is important to consider medicinal plants as meta organisms comprising the plant and its microbiome. Viewing them in this way reveals a large untapped source of biologically active compounds and microbes that could have possible uses in pharmaceutical, agricultural and modern medicinal fields. Therefore, further investigations are required to fully utilize this extensive resource for the benefit of humanity.

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