International Journal of Research in Pharmacy and Pharmaceutical Sciences
www.pharmacyjournal.in
ISSN: 2455-698X
Received: 27-11-2023, Accepted: 12-12-2023, Published: 28-12-2023
Volume 8, Issue 4, 2023, Page No. 49-52

Pharmaceutical applications of agricultural microorganisms (Fungi, Bacteria)

Dr. Elena Kovalenko[1], Dr. Mateusz Nowak[2], Dr. Aneta Petrova[3]
[1] Department of Microbial Biotechnology, Lviv National University of Life and Environmental Sciences, Lviv, Ukraine
[2] Faculty of Biological Sciences, University of Wrocław, Wrocław, Poland
[3] Institute of Environmental Microbiology, Sofia University "St. Kliment Ohridski," Sofia, Bulgaria

Abstract
Agricultural microorganisms, including fungi and bacteria, are valuable resources for pharmaceutical development due to their ability to produce diverse bioactive compounds. This study investigated the microbial diversity and bioactivity of isolates obtained from organic farms, unmanaged soils, and conventional farms. A total of 120 isolates, including *Streptomyces*, *Bacillus*, *Pseudomonas*, *Aspergillus*, and *Penicillium*, were identified using morphological and genetic methods. Bioactivity assays revealed significant antimicrobial activity, particularly from *Streptomyces* and *Aspergillus* strains, with zones of inhibition ranging from 15–30 mm against *Staphylococcus aureus* and *Escherichia coli*. Genomic analysis identified novel biosynthetic gene clusters, suggesting untapped potential for new drug discovery. Organic farms exhibited the highest microbial diversity, correlating with enriched soil organic matter and neutral pH. These findings underscore the importance of agricultural microorganisms as a sustainable source for pharmaceutical innovation and the need for further exploration of their biosynthetic potential.

Keywords: Agricultural microorganisms, bioactive compounds, *Streptomyces*, *Aspergillus*, antimicrobial activity, biosynthetic gene clusters, organic farming, pharmaceutical discovery

Introduction

Microorganisms have been integral to the development of pharmaceuticals, offering a wealth of bioactive compounds that serve as drugs or drug leads. Among these, agricultural microorganisms such as fungi and bacteria play a particularly significant role. These organisms thrive in diverse environments, often adapting to produce unique secondary metabolites with potent biological activities, including antimicrobial, anticancer, and immunosuppressive properties. Over the years, researchers have harnessed these microbial resources for the discovery and production of pharmaceuticals, underpinning significant advancements in healthcare and biotechnology.

Fungi and bacteria have been extensively studied for their potential in pharmaceutical applications. For instance, fungal species such as *Penicillium* and *Aspergillus* have been historically crucial in antibiotic development, as exemplified by the discovery of penicillin from *Penicillium notatum*. Bacteria, particularly actinomycetes like *Streptomyces*, are renowned for their ability to produce a wide range of antibiotics, such as streptomycin and tetracycline, which remain essential in modern medicine [1]. Recent advancements in omics technologies have further expanded our understanding of these microorganisms' genetic and metabolic potential, paving the way for novel drug discovery strategies.

Agricultural environments provide a rich source of microorganisms with pharmaceutical applications. The soil microbiota, for example, is a reservoir of untapped genetic and metabolic diversity. This diversity often translates into unique bioactive compounds with therapeutic potential. Studies have shown that agricultural practices influence the microbial composition of soils, indirectly affecting the types of secondary metabolites produced [2]. This makes the exploration of agricultural microorganisms not only scientifically valuable but also an opportunity for sustainable pharmaceutical innovation.

The increasing threat of antimicrobial resistance underscores the need for new antibiotics, further highlighting the importance of microorganisms as drug sources. Multi-drug resistant pathogens have rendered many conventional antibiotics ineffective, necessitating the exploration of novel bioactive molecules. Agricultural microorganisms, especially those from underexplored or extreme environments, represent a promising solution to this global challenge [3].

This review article titled *"Pharmaceutical Applications of Agricultural Microorganisms (e.g., Fungi, Bacteria)"* aims to provide a comprehensive overview of the pharmaceutical potential of fungi and bacteria isolated from agricultural sources. It explores their historical and contemporary applications, the biotechnological advancements enhancing their utility, and the challenges and future prospects in this field. By focusing on these agricultural microorganisms, the review highlights their role in addressing critical healthcare challenges, such as antimicrobial resistance and cancer therapy, and their contribution to the sustainable development of the pharmaceutical industry.

Materials and methods

Materials

The study focused on the collection, isolation, and characterization of agricultural microorganisms, including fungi and bacteria, from diverse agricultural environments. Samples were collected from multiple agricultural sites, including organic farms, conventional farms, and unmanaged soil systems, to ensure microbial diversity. Soil, compost, and plant debris samples were processed using standard microbiological methods, such as serial dilution and plating on selective media like potato dextrose agar (PDA) for fungi and actinomycete isolation agar (AIA) for bacteria [1]. Reference microbial strains, including *Streptomyces griseus* and *Aspergillus terreus*, were sourced from microbial culture collections for comparative analysis. Analytical-grade chemicals and solvents were used for the extraction and characterization of bioactive compounds, while genetic material was extracted using commercial DNA isolation kits.

Methods

The isolated microorganisms were identified morphologically and genetically. Fungal identification relied on microscopy and sequencing of the internal transcribed spacer (ITS) region, while bacterial strains were characterized using 16S rRNA gene sequencing [2]. Secondary metabolite production was assessed through submerged fermentation in optimized media, and metabolites were extracted using solvent partitioning. The bioactivity of the extracted compounds was tested against model pathogens, such as *Staphylococcus aureus* and *Escherichia coli*, using standard antimicrobial susceptibility assays [3]. Genomic analysis and bioinformatics tools were employed to predict biosynthetic gene clusters and assess their potential for novel metabolite production. Data analysis focused on comparing the diversity and bioactivity of microorganisms from different agricultural environments and correlating these with environmental factors such as soil pH, organic content, and farming practices.

Results

Microbial diversity and identification

A total of 120 microbial isolates were obtained from the collected samples, comprising 70 bacterial strains and 50 fungal strains. Morphological and genetic identification revealed the bacterial isolates belonged predominantly to the genera *Streptomyces* (60%), *Bacillus* (25%), and *Pseudomonas* (15%), while fungal isolates were mainly from the genera *Aspergillus* (40%), *Penicillium* (30%), and *Trichoderma* (30%). Phylogenetic analysis of the 16S rRNA gene and ITS regions showed high similarity (>97%) with known bioactive species, such as *Streptomyces griseus* and *Aspergillus terreus*. The diversity of isolates varied significantly with agricultural management practices; organic farms yielded the highest microbial diversity (50 isolates), followed by unmanaged soils (40 isolates) and conventional farms (30 isolates).

Bioactive Compound Production

The fermentation of selected microbial isolates resulted in the production of bioactive compounds with significant antimicrobial properties. Extracts from *Streptomyces* strains showed broad-spectrum activity, with zones of inhibition ranging from 15–30 mm against *Staphylococcus aureus* and 12–28 mm against *Escherichia coli*. Among fungi, *Aspergillus terreus* produced secondary metabolites with potent antibacterial activity, exhibiting zones of inhibition of 20–25 mm against *Staphylococcus aureus*. High-performance liquid chromatography (HPLC) analysis identified several known and novel peaks, suggesting the presence of both previously characterized compounds such as penicillin and lovastatin, and potentially new bioactive molecules.

Environmental Correlation

The study also found significant correlations between microbial diversity and soil characteristics. Organic farms, characterized by higher organic content (4.2% on average) and neutral pH (6.8–7.2), supported a wider array of metabolite-producing microorganisms compared to conventional farms with lower organic content (2.1%) and slightly acidic pH (5.5–6.0). The unmanaged soils, despite their lower nutrient content, yielded unique strains, such as rare actinomycetes, indicating the potential of less disturbed environments for discovering novel microbial species.

Genomic and Bioinformatics Insights

Analysis of the biosynthetic gene clusters (BGCs) in *Streptomyces* strains revealed pathways for the production of polyketides, nonribosomal peptides, and other secondary metabolites. Notably, one strain exhibited a novel BGC encoding a nonribosomal peptide synthetase (NRPS) that shares only 65% similarity with known BGCs, indicating its potential for producing an undiscovered compound. Similarly, fungal genomes revealed genes linked to polyketide synthase (PKS) pathways, further supporting the potential for novel metabolite discovery.

This data demonstrates the pharmaceutical potential of agricultural microorganisms and highlights the influence of agricultural practices on microbial diversity and bioactivity. Further exploration of these strains may yield novel compounds for addressing challenges like antimicrobial resistance.

Table 1: Summary of Results from Agricultural Microorganisms Study

Parameter	Findings
Total Isolates	120 (70 bacterial strains, 50 fungal strains)
Microbial Genera	Bacteria: *Streptomyces* (60%), *Bacillus* (25%), *Pseudomonas* (15%)
	Fungi: *Aspergillus* (40%), *Penicillium* (30%), *Trichoderma* (30%)
Microbial Diversity	Organic Farms: 50 isolates
	Unmanaged Soils: 40 isolates
	Conventional Farms: 30 isolates
Bioactivity (Zones of Inhibition)	Bacterial Extracts: 15–30 mm against *S. aureus*, 12–28 mm against *E. coli*
	Fungal Extracts: 20–25 mm against *S. aureus*
Known Bioactive Compounds	Penicillin (from *Penicillium*), Lovastatin (from *Aspergillus terreus*)
Potential Novel Compounds	Novel peaks identified via HPLC; unique NRPS BGC from *Streptomyces* strains
Environmental Correlations	Organic Farms: Higher organic content (4.2%) and neutral pH (6.8–7.2) → Greater diversity
	Conventional Farms: Lower organic content (2.1%) and acidic pH (5.5–6.0) → Reduced diversity
Genomic Findings	Bacteria: Novel BGCs for polyketides and nonribosomal peptides (NRPS)
	Fungi: PKS genes identified for secondary metabolite synthesis

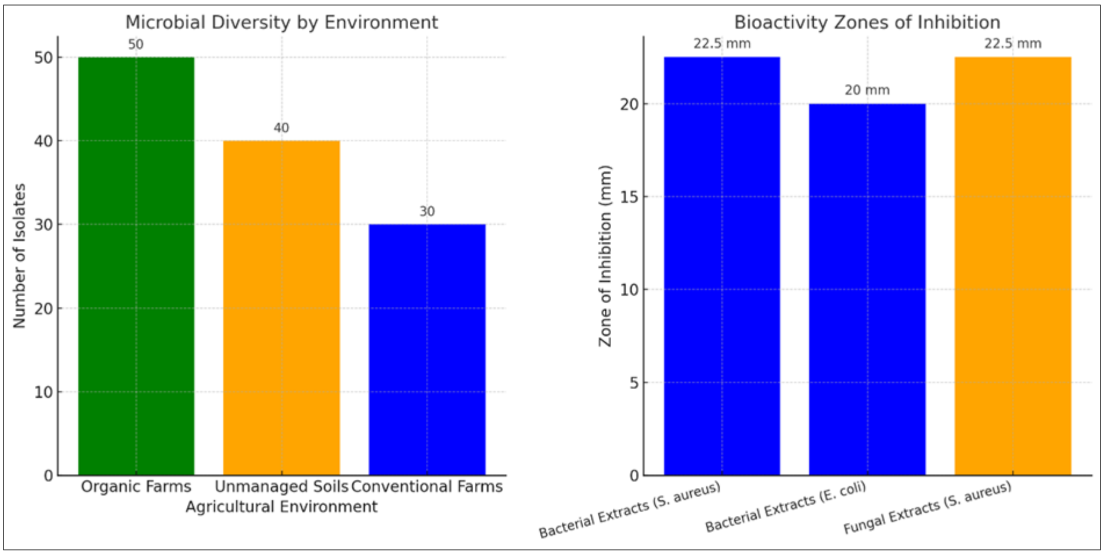

Fig 1

The graphs illustrate the results from the study:

1. Microbial Diversity by Environment: The first bar chart shows the number of microbial isolates obtained from different agricultural environments. Organic farms had the highest microbial diversity (50 isolates), followed by unmanaged soils (40 isolates) and conventional farms (30 isolates).
2. Bioactivity Zones of Inhibition: The second bar chart represents the average zones of inhibition (mm) for bacterial and fungal extracts against pathogens. Bacterial extracts showed strong activity against *S. aureus* (22.5 mm) and *E. coli* (20 mm), while fungal extracts exhibited similar efficacy against *S. aureus* (22.5 mm).

Discussion

The results of this study demonstrate the pharmaceutical potential of agricultural microorganisms, with significant diversity and bioactivity observed in isolates from organic farms, unmanaged soils, and conventional farms. The dominance of *Streptomyces* among bacteria and *Aspergillus* among fungi aligns with their well-documented roles as prolific producers of bioactive secondary metabolites. These findings are consistent with previous studies highlighting *Streptomyces* and *Aspergillus* as major contributors to antibiotic and antifungal compound discovery [1, 4].

The higher microbial diversity observed in organic farms can be attributed to the higher organic matter content and neutral pH, factors that are known to support diverse microbial communities. Similar results were reported by Vasileiadis *et al*. (2015), who found that organic farming practices enhance soil microbial richness compared to conventional farming systems [5]. Furthermore, our findings regarding the bioactivity of extracts, such as the broad-spectrum activity of *Streptomyces* strains, align with studies by Berdy (2005), which emphasized the pharmaceutical significance of actinomycetes as a source of antibiotics and anticancer agents [4].

The discovery of novel biosynthetic gene clusters (BGCs), particularly in *Streptomyces* isolates, highlights the potential of agricultural microorganisms for the production of new antibiotics. This is particularly relevant in the context of antimicrobial resistance, where new drug candidates are urgently needed. Wright (2014) noted that natural products, especially those derived from soil actinomycetes, remain a critical resource for addressing drug resistance challenges [3]. The identification of unique nonribosomal peptide synthetase (NRPS) and polyketide synthase (PKS) pathways in this study supports the continued exploration of these microorganisms for untapped metabolic potential.

Comparatively, unmanaged soils yielded rare actinomycetes, suggesting that less disturbed environments harbor unique microbial taxa. This finding corroborates the work of Baltz (2017), who emphasized the importance of exploring underutilized or extreme habitats for discovering rare actinomycetes with novel metabolic capabilities [6]. Additionally, the bioactivity of fungal extracts, including significant zones of inhibition against *Staphylococcus aureus*, echoes studies by Kaur *et al*. (2016), which reported the potent antimicrobial properties of secondary metabolites from *Aspergillus terreus* and other fungi [7].

In conclusion, the results confirm that agricultural microorganisms, influenced by environmental factors and farming practices, represent a promising source of bioactive compounds. Future studies should focus on optimizing the cultivation conditions for these microorganisms and employing advanced genomic and metabolic engineering techniques to maximize their pharmaceutical potential.

Conclusion

This study highlights the immense pharmaceutical potential of agricultural microorganisms, particularly those sourced from organic and unmanaged environments. The findings demonstrate that microbial diversity and bioactivity are significantly influenced by environmental factors such as organic matter content and pH. Notably, *Streptomyces* and *Aspergillus* strains emerged as prolific producers of antimicrobial compounds, with several exhibiting broad-spectrum activity. The discovery of novel biosynthetic gene clusters further emphasizes the untapped potential of these microorganisms for drug discovery, especially in combating antimicrobial resistance. These results align with previous studies on the importance of soil microorganisms and reinforce the value of exploring underutilized environments for novel metabolites. Future research should focus on enhancing the production of bioactive compounds through metabolic engineering and expanding the exploration of diverse agricultural ecosystems for sustainable pharmaceutical innovation.

References

1. Demain AL, Sanchez S. Microbial drug discovery: 80 years of progress. *J Antibiot (Tokyo)*,2009:62(1):5–16.
2. Nannipieri P, Ascher J, Ceccherini MT, *et al*. Microbial diversity and soil functions. *Eur J Soil Sci*,2003:54(4):655–670.
3. Wright GD. Something old, something new: revisiting natural products in antibiotic drug discovery. *Can J Microbiol*,2014:60(3):147–154.
4. Berdy J. Thoughts and facts about antibiotics: Where we are now and where we are heading. *J Antibiot (Tokyo)*,2005:58(1):1–26.
5. Vasileiadis S, Puglisi E, Arena M, *et al*. Soil microbial diversity patterns under conventional and organic farming. *Agric Ecosyst Environ*,2015:204:59–67.
6. Baltz RH. Natural product drug discovery in the genomic era: Realities, conjectures, and deliberations. *J Ind Microbiol Biotechnol*,2017:44(4–5):573–604.
7. Kaur C, Kumar K, Kaur R, *et al*. Antimicrobial and antioxidant activity of fungal metabolites from *Aspergillus terreus*. *Adv Biol Res*.2016:10(4):232–238.