RESEARCH PAPER

Innovative Synergy between Medicinal Plants and Metal Complexes for Suppressing Potato Wilt Disease.

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ABSTRACT

A synergistic effect was achieved by combining previously produced metal complexes with extracts from medicinal herbs known for their inherent antifungal properties, including *Carica papaya, Moringa oleifera, Saraca indica,* and *Rauwolfia serpentina* L. A comparative analysis showed that the antimycotic activity of medicinal plant extracts combined with metal complexes was greater than that of either plant extracts or individual metal complexes. Notably, when coupled with extracts of *Moringa oleifera* and cadmium ferrocyanide, these compounds had the most antimycotic effects against *Fusarium oxysporum.* These results highlight the potential of metal complexes and medicinal plant extracts as long-term disease treatment strategies by demonstrating how their synergistic interactions enhance antifungal activity.

Keywords: Synergistic effects, medicinal plants, transition metal ferrocyanides, *Fusarium oxysporum.*

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INTRODUCTION

The usage of medicinal plants is becoming more and more common worldwide as an alternative treatment for a variety of illnesses. The vast quantity of plant species with therapeutic qualities has led to the creation of some sciences, such as medical herbalism, which has enabled the widespread use of traditional medicine in several nations (23).

Depending on where the plant is used and which social groups use it, different medicinal plants have different traditional purposes. This article provides an overview of medicinal plants and their worldwide use. Scientific sources and databases provided the information. A qualitative investigation on the traditional use of medicinal herbs at the exact locations where they are sold is also presented in a case study of an indigenous community. In the primary healthcare system in communities with limited resources, traditional medicine continues to be the most accessible and reasonably priced form of therapy. In indigenous medical systems around the world, medicinal plants play a significant role. Research and development of natural drugs can benefit greatly from ethno botany (13).

Many medications that are marketed as "traditional herbal medicines" have undoubtedly been used for a long time, as implied by the term "traditional" use. Anti-inflammatory, antiviral, anticancer, antimalarial, and analgesic qualities are among the many therapeutic benefits linked to medicinal plants(13-14).

The *Carica papaya* is a member of the *Caricaceae* family (Fig.-1), which includes various species that have been used as remedies for a range of illnesses. Papain, chymopapain, cystatin, tocopherol, ascorbic acid, flavonoids, cyanogenic glucosides, and glucosinolates are among the numerous active ingredients found in papaya leaves that have been demonstrated to raise blood levels of antioxidant power and lower lipid peroxidation. As resistance to current treatments is growing; plants that have activity against human pathogenic fungus are of interest(18). Post-harvest infections, which directly cause losses of up to 40% during storage and transportation, restrict the production and quality of papaya in India. These illnesses, which are mostly brought on by several fungus, primarily *Colletotrichum gloeosporioides*, *Rhizopus stolonifer*, and *Fusarium* spp., include anthracnose, white rot, and fruit dry rot. For fruit fungus attacks to be properly controlled, synthetic fungicides are necessary but some of these fungicides are harmful to the environment and to people or animals that come into contact with them, and when fungi become resistant to them as a result of incorrect administration, their effectiveness may be diminished (9,15).

Originating in Africa, Arabia, South Asia, South America, the Himalaya area, India, Pakistan, the Pacific, and the

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Caribbean Islands, *Moringa oleifera* is a member of the *Moringaceae* family(Fig.-2). Many tropical and subtropical places across the world have naturalized *Moringa oleifera*, which is known by a variety of names, including "Mother's best friend," "drumstick tree," "ben oil tree," "horseradish tree," and "miracle tree" "Drumstick" is a common name for *Moringa oleifera*. The sub-Himalayan region is home to this small to medium-sized tree, which is around 10 meters tall (1).

Additionally, the plant has been shown to be hepatoprotective against antitubercular medications including rifampicin and isoniazi. The anti-inflammatory, antibacterial, diuretic, antibiotic, hypotensive, and diuretic effects of *Moringa oleifera* are also being investigated.

Niaziminin, which has a structural need to prevent tumor promoter-induced Epstein Barr virus activation, and an immune-enhancing polysaccharide have been reported from the leaves. There have been reports of analgesic effects from the alcoholic extract of *Moringa oleifera* leaves. The plant has historically been used as a diuretic, expectorant, stimulant, and antispasmodic(2).

Traditional medicine has utilized *Saraca indica*, a member of the *Caesalpiniaceae* family(Fig.-3), to treat a range of illnesses. This plant contains a variety of phytochemical substances, such as glycosides, tannins, saponins, flavonoids, and sterols, in its leaves, stem, stem bark, flowers, pods, and seeds. Herbs are reported to have therapeutic properties in ancient texts like the Sushrut Samhita and Charak Samhita, which are regarded as encyclopedias of ayurvedic medicine (17,21). Numerous bacterial species, such as Escherichia coli, Staphylococcus aureus, and Bacillus subtilis, are susceptible to the broad-spectrum antibacterial action of *Saraca indica*, especially its bark extracts. Research has indicated that both aqueous and ethanolic extracts have antibacterial properties, however ethanolic extracts frequently exhibit more activity. Additionally, methanolic extracts have potent antibacterial properties against fungus and bacteria (20-21).

One of the best therapeutic plants is *Rauwolfia serpentina Apocynaceae* family (Fig.-4), which yields beneficial alkaloids like reserpine in alternative medical systems; several portions of this plant are utilized to heal human illnesses(4). For hundreds of years, people in India have employed the root of *Rauwolfia serpentina* to treat a variety of unconnected illnesses. The plant has received widespread recognition as a helpful treatment for high blood pressure since 1949, when the author published a clinical report in English on the use of *Rauwolfia serpentina* therapy in fifty patients of essential hypertension(19,24).

Figures 1-4. Leaves of *Carica papaya, Moringa oleifera, Saraca indica, and Rauwolfia serpentina*

The filamentous fungus *Fusarium*. is frequently found in the environment and is thought to be non-pathogenic Numerous mycotoxin-producing plant pathogens, opportunistic human pathogens, and other agronomically significant pathogens are found in the filamentous fungal genus *Fusarium*. A genus of ascomycetous fungi called Penicillium is crucial to the creation of food, medicine, and the environment.The fungi Trichoderma species are widely distributed and can be found in a variety of soil types, manure, and decomposing plant matter (6).

A review of the literature reveals that there are only few studies on the interaction of metal ferrocyanides with natural antifungals or the potential medical uses of their complexes. Research on the therapeutic uses of metal ferrocyanide complexes in natural antifungals appears to be quite intriguing (5,7).

Such researches were attempted in light of this. Nonetheless, because metal ferrocyanides are thought to be superior ion exchangers and absorbents, they ought to interact with these secondary metabolites as they contain organic compounds that might interact with other chemical species. In order to have a higher impact on fungal development, the complex that forms should be more reactive(3,11,8).Examining the antimicrobial qualities of transitional metal complexes in conjunction with secondary metabolites present in medicinal plants to combat bacterial and fungal infections is the main objective of this research. Evaluating the antibacterial synergy between transitional metal complexes and secondary metabolites from medicinal plants is the specific aim of the study. To learn more about how these combinations work against microbial pathogens, investigate their effectiveness, safety, and environmental impact as substitute treatments for microbial diseases. Here, we address how plant extracts and metal complexes work in concert to combat the fungus *Fusarium oxysporum*, which causes potato wilt. We also present scientific advancements that could aid in overcoming obstacles in the natural plant-based medication discovery process.

We identify possible future directions for the discovery of natural plant-based drugs in the final section.

2. MATERIAL AND METHOD:

2.1 Collection of fungal cultures

In August 2024, *Fusarium oxysporum*, a fungus that causes late blight in potatoes, was purchased from the Central Potato Research Institute (CPRI), located in Modipuram, Meerut, India. For two days, the pathogen was grown at 25–30°C on potato dextrose agar (PDA) medium.

2.2 Collection of medicinal plants

The Botanical Garden of Sardar Vallabhbhai Patel University of Agriculture and Technology, Meerut U.P., India, which is situated at 247 meters above sea level and has a latitude range of 29°04'29''N-29°04'28''N, was the source of samples of *Carica papaya*, *Moringa oleifera*, *Saraca indica*, and *Rauwolfia serpentina* leaves in March and April of 2024. At 77°42'29''E -77°42'28''E is the longitude. The area experiences 775 millimetres of rainfall on average each year, with temperatures ranging from 2.5 to 43 degrees Celsius and relative humidity levels from 32 and 85%. For 15 to 20 days, the plant species were dried at 30 to 35 degrees Celsius in the shade. The leaves of each plant species were shade-dried, ground in a mixer, and then preserved. The dry leaf powder was extracted using four to five milliliters of methanol for each gram of plant material. All of these extracts were combined, and then flash evaporation was used to concentrate them at 40°C.

Synthesis of transition metal ferocyanides

To create these metal complexes, the Kourim approach (12) is used. Ferrocyanides of manganese, cobalt, nickel, copper, zinc, and cadmium were created using this process, and their identities were confirmed by X-ray diffraction analysis (SCXRD) results, magnetic susceptibility testing (Sherwood Scientific), and infrared spectra (KBR disc on Bio-red FTIR spectrophotometer) results already been published(19).

2.4 Antifungal activity of plant extracts with metal ferrocyanide complexes

The paper disc method (16) was used to test the antifungal activity. The most recent studies mixed metal complexes with extracts from therapeutic plants. After adding a specific medicinal plant extract (5 mg) and transition metal ferrocyanide (5 mg) to a sterile petri dish containing potato dextrose agar (PDA) media, fungal spores were sprayed over the entire bottom of the petri dish using an aspirator. A fresh extract and ferrocyanide metal are used to repeat the procedure. Growth percentage inhibition (%) is calculated using the Vincent formula (25) as (Cg-Tg)/Cg100. Tg denotes growth during therapy in millimetres, whereas Cg denotes growth under control in millimeters. Every experiment was run three times, and the results were interpreted using the average value (Table 1-2). Every experiment was run in triplicate, and the findings were interpreted using the average value.

2.5 Synergistic effect of medicinal plant extracts with metal complexes

Put 5 mg of metal ferrocyanide and 5 mg of plant extract onto a sterile petri plate. Using an aspirator, fungus spores were freely distributed throughout the petri plate's bottom. Other plant extracts and metal complexes were often combined using a similar technique.

2.6 Statistical analysis

SPSS Statistics IBM Base 22.0 was used to do the statistical analysis. To ascertain normality, the study employed Shapiro-Wilk tests, paired t-tests, and descriptive statistics. Descriptive statistics and the Shapiro-Wilk test were used to interpret and characterize the data in order to support the assumptions of the parametric approaches.

RESULT AND DISCUSSION

3.1 Antimycotic activity of plant extracts

The highest antimycotic qualities were found in the extracts of *M. oleifera* and *R. serpentina*, respectively, when the fungicidal activity of *C. papaya, M. oleifera, S. indica,* and *R. serpentina* was examined. Therefore, the following is a list of the plant extracts' antimycotic qualities in order of evaluation: *S. indica* > *C. papaya* > *R. serpentina* > *M. oleifera*

3.2 Antifungal activity of metal complexes only

Cd(II) and Ni(II) were determined to have the highest and lowest fungicidal characteristics, respectively, after the fungicidal activity of Mn-II, Co(II), Ni(II), Cu(II), Zn(II), and Cd(II) was examined, as shown in Table 1 and Figure 5.

Table-1 Antifungal activity of metal complexes

Metal complexes	*Fusarium Oxisporum*	
	Inhibition zone (mm)	Inhibition (%)
Mn (II)	10	47
Co (II)	9	45
Ni (II)	6	38
Cu (II)	17	69
Zn(II)	13	52
Cd(II)	19	81

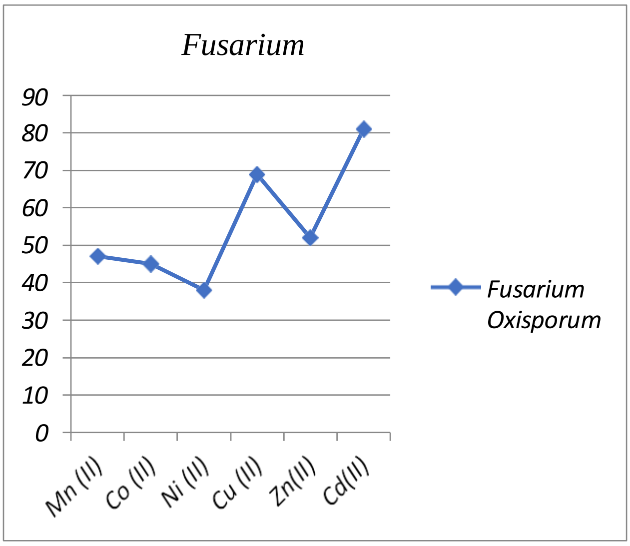

Fig.-5 Antifungal activity of metal complexes against *F.oxysporum*

Table-1 clearly shows that Cd (II) had the highest growth inhibition of 81% against *F. oxysporum*, Cu (II) had a considerable growth inhibition of 69%, and Mn-II and Co (II) had antmycotic potential of 38-52% against the same fungal pathogen.On the other hand, Ni (II) and Zn(II) were found to be less effective with growth inhibition, which is only up to 9-13% against fungal pathogen.Thus the antifungal activity of metal ferrocyanides was recorded in following order: Cd(II)>Cu(II) > ZnII)> Mn(II)> Co(II) >Ni(II).

3.3 Synergistic effect of medicinal plant extracts with metal complexes

The data provided in (Table -2) indicate that the combination of Cd(II) metal complex with plant extract *M. oleifera* of were recorded to have maximal fungicidal potential up to 19-31 mm growth inhibition against fungus taken for the current experiment.

While Co(II) and Cu(II) showed considerable antifungal capability up to 13-21 mm when combined with all of the plant extracts studied, Mn(II) showed better fungal growth inhibition (13-19mm) with all of the plant extracts. In contrast, the pairings of Ni(II) and Zn(II) with all of the plant extracts under study demonstrated the lowest antifungal activity in the 9-21 mm range.

Table-2 Synergistic effect of medicinal plant extracts with metal complexes

Meta l com plex es	*C. papaya*	*M. oleifera*	*S. indica*	*R. serpentine*
	Growth Inhibition zone (mm)			
Mn (II)	13	19	16	17
Co (II)	13	16	15	16
Ni (II)	9	12	10	12
Cu (II)	19	28	20	21
Zn (II)	15	21	17	19
Cd (II)	20	31	25	27

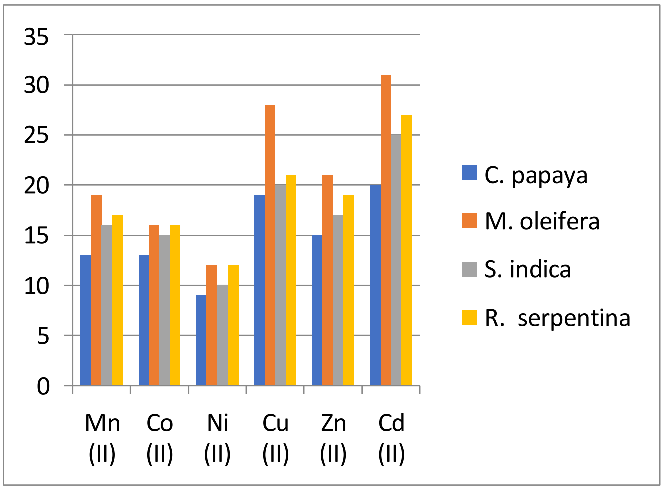

Fig-6Graphical representation of synergistic effect of medicinal plant extracts with metal complexes

Thus, the following sequence of antimycotic action was observed in the combination of transition metal complexes with medicinal plant extracts under study (refer to Table-2, Fig. 6):

1) Mn(II): *M. oleifera* > *R. serpentina* > *S. indica* > *C. papaya*

2) Co(II): *M. oleifera* > *R. serpentina* > *S. indica* > *C. papaya*

3) Ni(II): *M. oleifera* > *R. serpentina* > *S. indica* > *C. papaya*

4) Cu(II): *M. oleifera* > *R. serpentina* > *S. indica* > *C. papaya*

5) Zn(II): *M. oleifera* > *R. serpentina* > *S. indica* > *C. papaya*

6) Cd(II): *M. oleifera* > *R. serpentina* > *S. indica* > *C. papaya*

When only metal ferrocyanides are considered, Cd(II) and Ni(II) have the strongest and lowest antimycotic capabilities, respectively. However, secondary metabolites antimycotic activity is increased when they interact with metal ferrocynides. Furthermore, it was discovered that *M.*

oleifera extract with cadmium ferrocyanide and *C. papaya* extract with nickel ferrocyanide had the highest and lowest levels of fungicidal activity, respectively.

Thus, the current study's findings suggest that a combination of Cd(II) and *M. oleifera* extract could be used as an effective antimycotic agent for potato wilt disease. The findings demonstrated that these transition ferrocyanides are utilized to treat a wide range of pathogenic illnesses, and that Cu(II), Co(II), Cd(II) and Zn(II) might be used to investigate the likely reason of the synergistic action of bioactive chemical compounds discovered in medicinal plants. These findings suggest that these transition metal complexes can be applied as fungicides on their own or in conjunction with other plant-botanical fungicides to create environmentally benign fungicides that protect our environment and health from soil contamination.

3.4 Statistical analysis

A paired t-test was used to determine the significance of the mean difference between metal ferrocyanides and medicinal herbs. Value was considered and provided in (Table-3 & Fig.-7).

Table-3 Statistical analysis of Synergistic effect of medicinal plant extracts with metal complexes

Name of the Plant	Growth Inhibition against *Fusarium Oxisporum*		
	Mean	Standard deviation	Paired t-test value (p-value)
	7.85	3.97	Before Compare
Carica papaya	8.17	3.66	5.31 (< 0.001)
M. oleifera	15.68	4.02	17.02 (< 0.000)
R. serpentina	12.74	3.72	7.770 (< 0.000)
S. indica	9.523	3.45	8.010 (< 0.000)

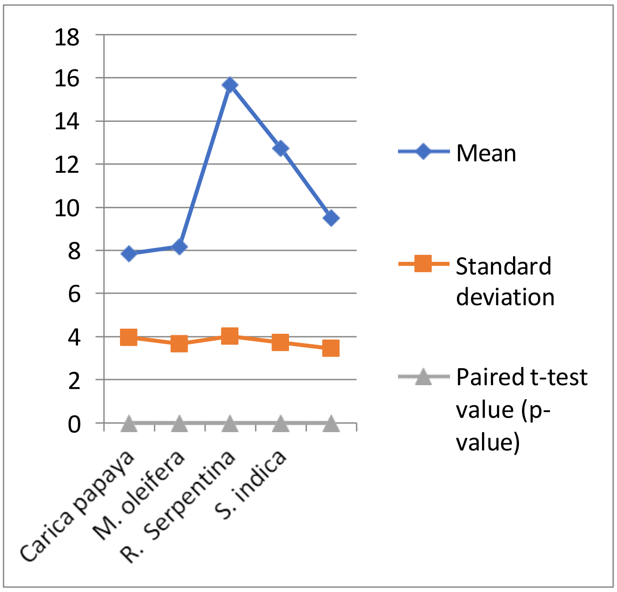

Fig.-7 Statistical analysis of Synergistic effect of medicinal plant extracts with metal complexes

The paired t-test results show a significant difference in fungal growth between *F. Oxisporum*, *C. papaya* (paired t-test value-5.42 (< 0.001) *M. oleifera* (paired t-test value-17.02 (< 0.000), *R. serpentina* (paired t-test value-7.770 (< 0.000) and *S. indica* paired t-test value-8.010 (< 0.000). Overall, we have found the highly significant p-value in all four medicinal plants extract and antimycotic action was seen in the combination of transition metal complexes with the help of statistical analysis.

CONCLUSION

Combination medicine therapy is not a novel concept, but innovative and useful uses of phytochemicals to develop safe and effective combination therapies may be key to the future of environmental safety and infectious disease control. Contrarily, synergism can be thought of as a form of combination therapy in which the activity of one component is significantly increased by the presence of another. Understanding synergism and its various forms may need a deep comprehension of statistical methods, molecular mechanics, and contemporary, enhanced technology. The most effective and commonly used bioactive substances for the treatment of infectious diseases were compiled in this article, along with any known mechanisms of action. Again, comprehensive details are provided about the shown synergistic benefits of several plant-derived bioactive compounds when combined with manufactured medications.

The ecology is deteriorating daily as a result of the frequent and ongoing use of synthetic pesticides to combat plant diseases. The aforementioned problem is presently being addressed by scientists in an effort to create a sustainable and environmentally friendly solution.

The findings of this study also point to the possibility of using metal complexes as fungicides.

Either alone or in conjunction with different secondary metabolites of plants, leading to the creation of safer, more eco-friendly fungicides that can shield our environment from future pollution of all kinds. In order to better understand the synergistic effect of synthetic chemicals and plant botanicals, it is hoped that future study would concentrate on creating innovative strategies for targeting harmful bacteria and fungus.

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DECLARATION

We certify that each author has made a substantial contribution to this Ms. No writer who contributed significantly to this was overlooked, Ms. We have complied with the ethical guidelines established by our respective organizations.

CONFLICT OF INTREST

The writers declare that there is no conflict of interest between them.

ETHICAL APPROVAL

The authors declare that the study was carried out following scientific ethics and conduct.

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