

## Exploring the Antimicrobial Potential of Naturopathic Therapies and Herbal Extracts Against Emerging Microbial Pathogens

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### Abstract

Antimicrobial resistance has emerged as a major global health concern, leading to reduced effectiveness of conventional antibiotics and antifungal drugs. The continuous rise of multidrug-resistant microbial pathogens has stimulated increasing interest in alternative therapeutic strategies derived from natural sources. Naturopathic therapies and herbal extracts contain diverse phytochemicals that exhibit significant antimicrobial potential through multiple biological mechanisms. This review aims to explore the antimicrobial efficacy of naturopathic therapies and plant-derived compounds against emerging microbial pathogens, with emphasis on phytochemical constituents, mechanisms of action, and modern technological approaches that enhance their therapeutic potential. A comprehensive literature review was conducted using peer-reviewed studies focusing on medicinal plants, phytochemicals, nanotechnology-based herbal formulations, and antimicrobial activities against resistant bacterial and fungal pathogens. Relevant experimental and mechanistic studies were examined to evaluate the effectiveness of plant-derived compounds and their role in combating microbial resistance. Numerous plant extracts and phytochemicals demonstrated broad-spectrum antimicrobial activity through mechanisms including disruption of microbial membranes, inhibition of biofilm formation, suppression of virulence factors, and interference with metabolic pathways. Additionally, nanotechnology-based formulations such as green-synthesized nanoparticles significantly enhanced the antimicrobial efficacy and stability of plant-derived compounds. These approaches showed promising activity against multidrug-resistant pathogens and emerging fungal species. Herbal extracts and naturopathic therapies represent promising alternatives or complementary strategies for managing infections caused by resistant microorganisms. Continued research focusing on mechanistic studies, advanced formulations, and clinical validation is essential to support the integration of plant-derived antimicrobial agents into modern therapeutic applications.

**Keywords:** Antimicrobial Resistance, Herbal Extracts, Naturopathic Medicine, Phytochemicals, Plant-Derived Antimicrobials

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### 1. Introduction

One of the most important health issues in the twenty-first century is antimicrobial resistance (AMR). Overuse and misuse of antibiotics in various fields, including medicine, agriculture, and veterinary medicine, have significantly contributed to the emergence of resistant microbial strains. This has significantly diminished the efficacy of many conventional antimicrobial drugs. Resistant microbial strains have been strongly associated with severe disease, hospitalization, and increased mortality. These factors emphasize the importance of developing alternative therapeutic drugs that are capable of effectively combating resistant microbial strains. Apart from mutations in microbial

strains, complex microbial communication systems such as quorum sensing play a vital role in regulating microbial resistance. Disruption of such systems is one of the most important areas in developing alternative antimicrobial drugs based on natural products and traditional medicine systems<sup>1</sup>.

Recent years have also seen the discovery of opportunistic fungal pathogens that have shown significant resistance to the most commonly used antifungal agents. Among these, *Candida auris* has gained significant importance due to its multidrug resistance and ability to survive in hospital environments, causing widespread outbreaks in hospitals and healthcare facilities around the world.

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Research on plant-based nanomaterials and phytochemical compounds has shown promising antifungal activities against these resistant strains, indicating that compounds derived from natural sources may prove to be effective against resistant strains of fungi and may replace conventional antifungal agents in the near future<sup>2</sup>. Similarly, research on naturally derived compounds that target fungal cell wall synthesis has identified new antifungal compounds with unique modes of action, indicating the potential of naturally derived compounds in combating new strains of fungal pathogens.

Natural products have traditionally played an important role in the discovery of antimicrobial compounds. Many traditional systems of medicine rely on plant-derived compounds for the treatment of infectious diseases, and they are also effective because they possess multiple modes of antimicrobial activity<sup>3</sup>. Herbal extracts have shown promise as effective inhibitors of microbial growth, disruption of cell structures, and immune system modulation. These properties are useful in the treatment of infections caused by drug-resistant pathogens, as plant-derived bioactive compounds can act on multiple cellular targets simultaneously, thereby reducing the chances of developing resistance<sup>4</sup>. These properties are advantageous over many conventional antibiotics that are capable of acting on only one molecular target at a time.

Essential oils and secondary plant metabolites have also garnered considerable attention from scientists due to their high anti-infective properties. Phenolic volatile compounds, which are present in essential oils, are highly active against various pathogens and can inhibit microbial growth, disrupt cell structures, and inhibit various enzyme systems of the pathogens. These compounds are effective against various microorganisms, ranging from bacteria, fungi, and viruses, and are useful for the development of alternative anti-infective formulations<sup>5</sup>.

The therapeutic value of botanical compounds has been extensively studied in relation to multidrug-resistant pathogens. Several phytochemicals, including those isolated from various plants used in traditional medicine, have been found to possess the ability to improve the efficacy of antibiotics, inhibit the formation of microbial biofilms, and restore sensitivity in drug-resistant microorganisms. Resistance-modifying agents derived from plants have been found to possess promising value in combating antimicrobial resistance by targeting the defense capabilities of microorganisms, not by killing them<sup>6</sup>. This method has emerged as a highly innovative strategy in the development of antimicrobial agents, as they may help to minimize the selection pressure that leads to the emergence of resistant microorganisms.

Besides traditional botanical agents, modern research has increasingly explored the integration of natural compounds with modern technology to enhance their antimicrobial efficacy. Novel delivery agents, including nano-phytochemicals and nanoparticles synthesized from various plant extracts, have emerged as highly

promising agents in combating drug-resistant microbial pathogens. These agents have been designed to improve the stability and efficacy of various botanical compounds, thus allowing for their targeted delivery to the site of infection.

Similarly, natural bioactive compounds have shown promising results in modulating the immune system of the host and maintaining the balance of microbes in the human body. Nutraceuticals and natural compounds have been studied for their potential in preventing infections and maintaining the balance of microbes in the human body<sup>7</sup>. In particular, integrative approaches to the use of plant compounds, probiotics, and nutraceutical compounds have been explored for their potential in effectively managing microbial infections and related inflammatory diseases in the human body.

In addition to their role in clinical infections, microbial resistance has also been recognized as a major concern in food safety and environmental health. Plant antimicrobial compounds have been explored for their potential in inhibiting foodborne pathogens in food processing systems. Natural antimicrobial compounds and plant extracts have shown inhibitory effects against various foodborne pathogens<sup>8</sup>. In particular, natural antimicrobial compounds have shown promising results in inhibiting foodborne diseases caused by various foodborne pathogens. Natural antimicrobial compounds have been used as an alternative to synthetic preservatives and antibiotics in food systems<sup>9</sup>.

In view of the rising global prevalence of antimicrobial resistance and limitations associated with conventional antimicrobial drugs, interest is rising in exploring naturopathic drugs and herbal extracts as alternatives for antimicrobial therapy<sup>10</sup>. With their unique chemical composition and ability to influence multiple microbial targets, medicinal plants hold promise for developing novel drugs that could combat emerging microbial threats. Hence, exploring plant-derived bioactive compounds and their therapeutic potential is critical for developing novel natural product-derived antimicrobial drugs.

## **2. Phytochemical Constituents Responsible for Antimicrobial Activity**

Plant-derived bioactive compounds are one of the most important sources of antimicrobial substances. Medicinal plants produce various secondary metabolites that serve as natural defense compounds against microbial invasion. These bioactive compounds have unique chemical structures and biological activities, thereby inhibiting microbial growth, affecting their metabolic pathways, and interfering with their virulence factors. The antimicrobial activity of plant extracts is mainly attributed to their ability to contain various types of phytochemical constituents such as phenolics, flavonoids, alkaloids, terpenoids, glycosides, etc. These constituents are responsible for the therapeutic effects of herbal drugs<sup>11</sup>.

Phenolic compounds are one of the most studied plant-derived antimicrobial substances. These compounds exhibit potent antioxidant and antimicrobial activities due to their ability to inhibit microbial cell membrane functions and vital metabolic pathways. Phenolic

compounds interact with microbial cell walls and membranes, thereby causing hyper-permeability and leakage of cell components. Various studies on plant-derived phenolic compounds have revealed their effectiveness against various antibiotic-resistant bacterial strains. These results show their potential in developing alternative antimicrobial therapies. Phenolic acids are also reported to inhibit enzyme systems that are vital for microbial growth.

Another group of phytochemicals with wide-ranging antimicrobial properties are flavonoids. Flavonoids are also ubiquitous in fruits, vegetables, and medicinal plants, with the ability to inhibit the growth of bacteria and the formation of biofilm<sup>12</sup>. Antimicrobial properties of flavonoids have been attributed to various mechanisms, which include inhibition of nucleic acid synthesis, disruption of the cell membrane of microbes, and disruption of energy metabolism pathways. Flavonoids have shown impressive results in combating fungal infections, especially *Candida sp.*, by inhibiting key cellular processes that are linked to fungal virulence and adherence<sup>13</sup>.

Phytosterols and other lipid-soluble phytochemicals also play a key role in the antimicrobial properties of medicinal plants. These compounds can interact with the cell membrane of microbes, thereby disrupting its fluidity and integrity, leading to destabilization of the cell membrane, which eventually leads to cell death. Studies on phytosterols, which are plant-derived steroids, have shown that they possess bactericidal and fungicidal properties against clinically relevant pathogens, indicating that they can be used as leads in

the development of antimicrobial drugs. Additionally, the cumulative effect of various active compounds present in one plant may lead to increased antimicrobial properties, hence increased efficacy of the drug.

In addition to flavonoids and sterols, the plant extracts contain a range of other alkaloids and terpenoids, which have been proven to have significant antimicrobial effects. The mode of action for these compounds is believed to be mediated through interference with microbial enzymatic systems<sup>14</sup>. For instance, terpenoids have been proven to inhibit microbial cell wall biosynthesis, as well as interfering with membrane-associated proteins, leading to impaired microbial viability. Some medicinal plant extracts, which contain terpenoids and alkaloids, have been proven to have inhibitory effects against Gram-negative and Gram-positive bacterial pathogens<sup>15</sup>.

In addition, the antimicrobial effects of phytochemicals are also mediated by the chemical diversity and structural complexity of the compounds. The chemical composition of most medicinal plants contains a range of bioactive compounds, which have synergistic effects in inhibiting microbial growth. The multifunctional mode of action for most phytochemicals is a major advantage over the limited mode of action for most antibiotics, which only inhibit microbial growth through a single mode of action. The multifunctional mode of action for most phytochemicals makes it difficult for microorganisms to develop resistance against these compounds. The major phytochemical compounds obtained from medicinal plants have been mentioned in Table 1.

**Table 1:** Major phytochemical constituents derived from medicinal plants and their antimicrobial mechanisms

Plant Source	Major Phytochemical Constituents	Target Microorganisms	Mechanism of Antimicrobial Action	Reference
<i>Carica papaya</i> leaves	Phytol, flavonoids, phenolic compounds	Antibiotic-resistant bacteria	Membrane disruption, inhibition of microbial metabolic enzymes	11
Sorghum ( <i>Sorghum bicolor</i> ) phenolic extracts	Phenolic acids, tannins	Liver abscess causing bacterial pathogens	Cell wall disruption and inhibition of bacterial growth pathways	12
<i>Vitex negundo</i>	Phenolic acids, flavonoids	<i>Candida albicans</i>	Anti-biofilm activity and inhibition of fungal adhesion	13
<i>Alkanna tinctoria</i> root extracts	Alkannin derivatives, naphthoquinones	Multidrug-resistant <i>Candida</i> species	Oxidative stress induction and fungal membrane damage	14
<i>Clauseana anisata</i> fruit	Phytosterol esters, furanocoumarins	Clinical bacterial and fungal pathogens	Membrane destabilization and enzyme inhibition	15

Overall, phytochemicals derived from medicinal plants represent promising candidates for the development of novel antimicrobial agents. Their diverse mechanisms of action, combined with their ability to target multiple microbial pathways, make them valuable tools in addressing the growing challenge of antimicrobial resistance. Continued investigation into the antimicrobial properties of plant-derived compounds may facilitate the discovery of new therapeutics capable of combating emerging microbial pathogens.

### 3. Antibacterial Activity of Medicinal Plants

Medicinal plants have traditionally been recognized as important sources of antibacterial substances. Various traditional systems of medicine use plant-derived antibacterial substances for the treatment of various bacterial infections. Recent scientific studies have confirmed the antibacterial potential of various plant-derived substances. Plant-derived antibacterial substances have shown efficacy against a wide range of

pathogenic microorganisms, including multidrug-resistant pathogenic bacteria. Various plant-derived antibacterial substances have been reported to exert their antibacterial effects by various mechanisms, such as inhibiting microbial growth, disrupting microbial cell structures, and affecting microbial virulence factors.

Certain medicinal plants have shown significant antibacterial potential against various pathogenic bacteria. Various studies have reported that plant-derived antibacterial substances inhibit the growth and biofilm formation of various pathogenic bacteria, such as *Staphylococcus aureus* and *Enterococcus faecalis*. The antibacterial potential of this plant is due to the presence of certain bioactive substances that inhibit microbial adhesion and biofilm formation<sup>16</sup>. These microbial adhesions and biofilm formations are critical for microbial colonization. Biofilm formation is one such critical microbial process that is often associated with antimicrobial resistance.

On the other hand, plant extracts that contain polyphenolic compounds have been shown to have antibacterial properties. For example, studies involving various species of medicinal plants that are rich in polyphenolic compounds have been shown to have antibacterial effects against gastrointestinal pathogens. Such studies have demonstrated that the plant extracts can cause damage to the bacterial cell wall, inhibit enzymes, and reduce the viability of the microbes. Such findings have demonstrated the potential of various compounds that are derived from plants to act as alternatives in addressing bacterial infections that have developed resistance to various antibacterial agents<sup>17</sup>. Several traditional medicinal plants that are used in herbal medicine have been shown to have antibacterial properties. For example, *Aegle marmelos* has been shown to have inhibitory effects against various pathogens that cause oral infections. For instance, the

bioactive compounds that are present in the plant have been shown to have effects against the virulence factors that are responsible for bacterial adhesion to the host.

Previous studies carried out on various medicinal plants, including *Prunus cerasoides*, have demonstrated considerable antibacterial activity against various bacterial strains. Compounds that have been isolated from the stem bark of *Prunus cerasoides* have been reported to inhibit various pathogenic microorganisms. Such inhibitory effects have been attributed to the disruption of the metabolic process and integrity of the bacterial cell membrane<sup>19</sup>. Natural compounds that have been isolated from traditional herbal remedies have been reported to exhibit considerable antibacterial effects against various bacterial strains, including those that cause oral infections.

Herbal compounds, including miswak, black seed, and Aloe vera, have been reported to exhibit considerable antimicrobial effects against various oral pathogens that cause dental infections. Such herbal compounds have been reported to contain compounds that can inhibit bacterial growth and prevent microbial colonization<sup>18</sup>. The antimicrobial effects of herbal compounds have been attributed to their potential use in the prevention and treatment of various bacterial infections.

The antibacterial properties of medicinal plants are of significant importance when considering the rising problem of antimicrobial resistance. This is because the antibacterial compounds found in medicinal plants are comprised of more than one compound that targets different bacterial targets. This makes it less possible for resistance to develop. Additionally, medicinal plant-derived antibacterial compounds are less toxic and more biocompatible than synthetic compounds. Several medicinal plants show promising antibacterial properties against pathogenic bacteria through growth inhibition and biofilm suppression (Table 2).

**Table 2:** Antibacterial activity of medicinal plant extracts

Medicinal Plant	Type of Extract	Target Bacterial Pathogens	Observed Antimicrobial Effect	Reference
<i>Murraya koenigii</i>	Methanolic extract	<i>Staphylococcus aureus</i> , <i>Enterococcus faecalis</i>	Inhibition of bacterial growth and biofilm formation	16
<i>Origanum majorana</i> , <i>Salvia officinalis</i> , <i>Ribes nigrum</i>	Ethanollic extracts	Digestive bacterial pathogens	Polyphenol-mediated antibacterial activity	17
<i>Aegle marmelos</i>	Plant extract	<i>Porphyromonas gingivalis</i>	Suppression of bacterial adhesion and virulence factors	18
<i>Prunus cerasoides</i>	Stem bark extract	Gram-positive and Gram-negative bacteria	Growth inhibition through metabolic interference	19
Miswak, <i>Nigella sativa</i> , <i>Aloe vera</i>	Herbal extracts	Oral pathogens	Reduction of microbial proliferation and oral biofilm formation	20

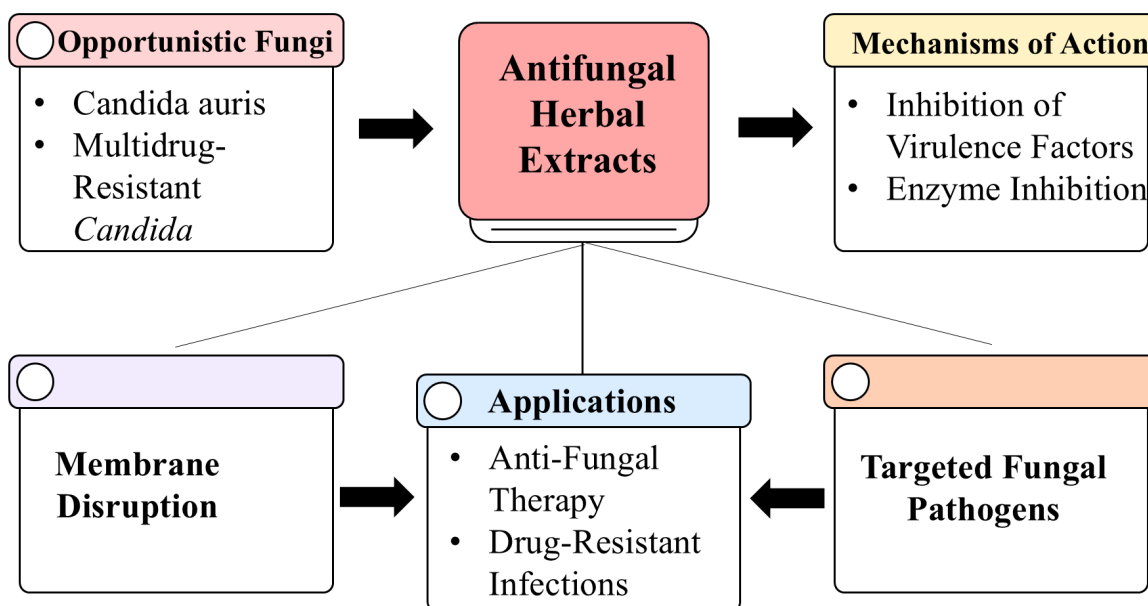
Overall, medicinal plants represent an important reservoir of antibacterial compounds with potential applications in modern medicine. Continued research on plant-derived antibacterial agents may contribute to the development of novel therapeutic strategies for

managing infections caused by multidrug-resistant bacteria.

#### 4. Antifungal Herbal Extracts Against Emerging Pathogens

Fungal infections have risen in recent decades, especially in immunocompromised patients. Novel fungal pathogens, such as *Candida auris*, have emerged and are difficult to manage due to their multidrug resistance and ability to survive in the environment<sup>19</sup>. As a result, various studies have investigated the antifungal properties of herbal compounds and their ability to combat fungal pathogens. Herbal compounds have shown various modes of action that can inhibit the growth of fungi and interfere with the virulence factors of pathogenic fungi. Herbal compounds have shown promising antifungal properties against resistant fungal pathogens. Bio-oil fractions, which are derived from biomass of tropical plants, have been reported to inhibit the growth of *Candida auris*<sup>20</sup>. This indicates that herbal compounds have the ability to combat emerging fungal pathogens. Bio-oil fractions may interfere with the cell membrane of fungal pathogens, causing dysfunction and inhibiting the growth of fungi. Several plant compounds have also shown antifungal properties by targeting specific enzymes or pathways in fungal metabolism. For example, some plant compounds have shown the potential to inhibit the enzyme dihydrofolate reductase in *Candida auris*. This enzyme plays a critical role in fungal metabolism<sup>21</sup>. Inhibition of this enzyme can significantly impair fungal metabolism, thereby affecting the growth and survival of the fungal pathogen. Inhibition of specific enzymes

in fungal metabolism can thus prove to be an effective way to control fungal infections. In this regard, traditional herbal formulations have also been tested for their antifungal properties<sup>22</sup>. Some plant-based decoctions have shown the potential to impair the energy metabolism of fungal pathogens. For example, some plant-based decoctions have shown the potential to impair the enzymes in the metabolic pathway of fungal pathogens. This can have a significant impact on fungal growth and pathogenesis. For example, impairment of the enzyme isocitrate lyase in fungal pathogens can prove to be an effective way to control fungal infections using plant-based decoctions. Natural plant extracts have also shown antifungal properties. Natural plant extracts contain essential oils that have shown the potential to inhibit fungal colonization<sup>23</sup>. Besides their antifungal properties, some plant extracts have been shown to have anti-virulence properties that reduce fungal virulence<sup>24</sup>. For example, gall extracts from some medicinal plants have been shown to have rapid antifungal and bactericidal properties against some fungal and bacterial pathogens that cause respiratory and oral infections. These plant extracts have been shown to reduce the virulence of the microbes, thereby improving the outcome of therapy<sup>25</sup>. Plant extracts have been shown to have antifungal properties through various biological mechanisms (Figure 1).



**Figure 1:** Antifungal activity of herbal extracts against opportunistic fungal pathogens and their mechanisms of action. The rise in the occurrence of drug-resistant fungal pathogens has also emphasized the need to search for alternative antifungal drugs. This is due to the fact that plant-derived compounds have several merits, which make them potential candidates for the development of antifungal drugs.

### 5. Anti-virulence and Anti-biofilm Activities of Plant-Derived Compounds

Microbial virulence factors have been identified to have a significant effect in the establishment and maintenance

of infections. Virulence factors include microbial toxins, adhesins, quorum sensing, and biofilm formation. They have been identified to have a significant effect in the establishment and maintenance of infections. In recent

years, however, there has been increased emphasis placed on the use of plant compounds that have the ability to inhibit microbial virulence instead of killing the microorganisms. Anti-virulence approaches have been identified to have significant advantages, including the inhibition of resistance and the reduction of pathogenicity. Several medicinal plants and compounds have been identified to have the ability to inhibit the virulence-related processes in pathogenic microorganisms.

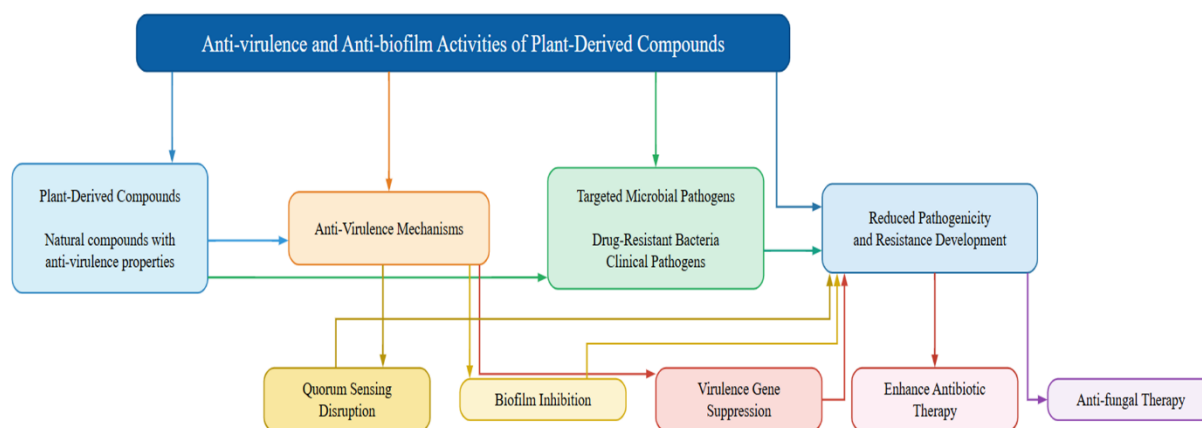
Biofilm formation has been identified to be one of the virulence-related processes in microorganisms. Biofilms have been identified to be complex communities of microorganisms that are embedded in a matrix<sup>26</sup>. They have been identified to have the ability to evade host immune responses and antimicrobial agents. Several plants have been identified to have the ability to inhibit biofilm formation.

Quorum sensing inhibition is another significant mechanism through which plant extracts are seen to influence the reduction of microbial virulence. Quorum sensing is essentially a communication mechanism of bacterial populations that regulate gene expression based on density. This mechanism enables bacterial populations to regulate the production of virulence factors, biofilms, and other bacterial toxins. It has been established that certain plant extracts are capable of

interfering with quorum sensing, thereby affecting the virulence of bacterial pathogens. The extracts of rambutan fruit peels are capable of inhibiting quorum sensing and biofilms of *Vibrio campbellii*, which makes them significant potential anti-virulence compounds for the control of microbial pathogens<sup>27</sup>.

Plant-derived compounds are also capable of inhibiting the gene expression of virulence factors responsible for bacterial pathogenicity. The extracts of *Saxifraga stolonifera* are capable of exerting antibacterial and anti-virulence effects on *Pseudomonas aeruginosa*, which is commonly responsible for hospital-acquired bacterial infections. The extracts inhibit the gene expression of virulence factors of the pathogen, thereby reducing its pathogenic potential<sup>28</sup>.

The extracts of herbs might also affect the colonization and adhesion processes of microbes. It has been found that marjoram extracts are effective in the down-regulation of genes that are involved in the adhesion, colonization, and production of toxins of *Pasteurella multocida*. By inhibiting these virulence factors of the pathogen, the plant extracts are effective in reducing the pathogenicity of the bacteria<sup>29</sup>. The adhesion of microbes to host tissues is an important process that needs to be targeted to inhibit the colonization of pathogens. The plant extracts are effective in inhibiting the virulence of resistant pathogens (Figure 2).



**Figure 2:** Anti-virulence and anti-biofilm mechanisms of plant-derived compounds targeting resistant microbial pathogens

In addition, there are plant extracts that possess both antimicrobial and anti-inflammatory activities, which might be beneficial for effective control of infections. The extracts of *Maranta arundinacea* have been found to possess antimicrobial activity against *Campylobacter* species, as well as modulating the inflammatory response of infected host cells<sup>30</sup>. This will be beneficial as it will not only control the pathogens but will also protect the host from the effects of inflammation.

## 6. Nanotechnology-Based Herbal Antimicrobials

The application of nanotechnology with natural products has provided new avenues for the creation of effective antimicrobial therapies. Nanotechnology has

allowed scientists to synthesize nanoparticles with the help of natural extracts, which have shown increased antimicrobial efficacy, stability, and targeted delivery of active compounds. These plant-mediated nanoparticles are also termed green synthesized nanoparticles, which are the combination of the biological properties of phytochemicals and the unique physicochemical properties of nanoparticles. The most used nanoparticles for antimicrobial purposes are silver nanoparticles synthesized by various plant extracts, which have shown increased antimicrobial efficacy against bacteria and fungi by interacting with the cell membrane of the microbes and inhibiting their growth. It has also been shown that silver nanoparticles synthesized by

medicinal plant extracts are capable of inhibiting the growth of multidrug-resistant microbes, even those that are resistant to fungal pathogens like *Candida auris*<sup>31</sup>. The size of the nanoparticles has also allowed them to be more efficient against microbes by increasing the surface area of the particles.

Copper oxide nanoparticles that are synthesized through plant-mediated methods have also shown significant antimicrobial potential. The nanoparticles are capable of entering the cell walls of microorganisms and disrupting cellular components such as proteins and DNA. The green synthesis of copper oxide nanoparticles using plant extracts has shown potential as an effective therapy against multidrug-resistant Gram-negative pathogens<sup>32</sup>.

The use of plant-mediated methods of nanoparticle synthesis has also shown advantages over other methods, such as those related to sustainability and biocompatibility. The chemical methods of nanoparticle synthesis are known to use toxic chemicals, whereas green synthesis methods use plant extracts as reducing and stabilizing agents. For example, copper oxide nanoparticles that were synthesized using *Ficus pumila* extracts showed potential as multifunctional biomaterials, including antimicrobial potential against pathogenic microorganisms<sup>33</sup>.

Advanced nanoparticle systems formulated from plant extracts have also been explored with regards to their improved antimicrobial properties. Nanoparticle systems formulated from *Pelargonium graveolens* extracts have shown antibacterial properties against

different pathogenic microorganisms through different mechanisms, such as membrane disruption and interference in their metabolism<sup>34</sup>. These types of nanoparticles may also be tested using molecular docking techniques to determine their interactions with phytochemicals and microorganisms.

Aside from silver and copper-based nanoparticles, different types of artificial nanoparticle systems formulated from plant extracts have been developed to improve their antimicrobial properties. Artificial neural network-optimized cysteine-conjugated silver nanoparticles have shown potent antibacterial properties against different pathogenic bacterial strains causing urinary tract infections in humans<sup>35</sup>. This type of study shows how artificial intelligence techniques may be used in improving nanoparticle synthesis and their antimicrobial properties.

Nanotechnology-based herbal antimicrobials have shown some advantages over traditional antimicrobial agents. These nanoscale antimicrobial agents improve the stability and bioavailability of plant-based compounds. In addition, nanoscale antimicrobial agents can target specific sites of infection. Moreover, nanoscale antimicrobial agents can act on several targets of microbes, including their membranes, enzymes, and genetic material. This reduces the chances of resistance development in microbes. Some recent findings have shown that plant-mediated nanoparticles can significantly improve antimicrobial activities against resistant microbial agents (Table 3).

**Table 3:** Plant-mediated synthesis of nanoparticles and their antimicrobial effects

Plant Material Used for Synthesis	Nanomaterial Produced	Target Microbial Pathogens	Key Antimicrobial Mechanism	Reference
Trans-Himalayan plant extracts	Silver nanoparticles	Drug-resistant <i>Candida auris</i>	Membrane damage and intracellular protein disruption	31
<i>Citrus pseudolimon</i>	Copper oxide nanoparticles	Multidrug-resistant Gram-negative bacilli	Reactive oxygen species generation and DNA damage	32
<i>Ficus pumila</i>	Copper oxide nanoparticles	Bacterial pathogens	Cell wall penetration and oxidative stress induction	33
<i>Pelargonium graveolens</i> extract	Silver chloride and silver chromium nanoparticles	Pathogenic bacteria	Membrane permeability alteration and metabolic disruption	34
Plant-mediated synthesis	Cysteine-conjugated silver nanoparticles	<i>Staphylococcus nepalensis</i>	Protein denaturation and enzyme inhibition	35

Overall, the combination of nanotechnology and plant-derived bioactive compounds represents a promising strategy for developing next-generation antimicrobial therapies capable of combating multidrug-resistant pathogens.

### 7. Natural Product Nanocomposites and Advanced Antimicrobial Formulations

The recent advances in the field of biomedical research have been directed towards the development of

innovative antimicrobial formulations that incorporate natural compounds with advanced biomaterials. This will enhance the therapeutic activity of plant-derived antimicrobial compounds. Natural product-derived nanocomposites and bioengineered materials have been considered to be potential candidates in the prevention of infectious diseases by multidrug-resistant pathogens. Nanofiber-based antimicrobial materials have been considered to be potential candidates in the prevention of infectious diseases due to their ability to deliver

bioactive compounds directly to the target sites of infection. Natural polymers with plant-derived antimicrobial compounds have been used to prepare nanofibrous wound dressing materials that can prevent microbial colonization. For example, curcumin-derived nanocomposites have been used to prepare pectin nanofibers, which have been considered to be effective in inhibiting multidrug-resistant pathogens that cause chronic wound infections<sup>36</sup>.

Another promising area for the development of antimicrobial materials includes the creation of antimicrobial nanofibers, which combine natural compounds with synthetic biomaterials. These advanced wound-healing systems have the capability to inhibit microbial growth while preventing biofilm formation. Research has proven that using these nanofiber-based wound-healing systems, which contain natural antimicrobial agents, can improve wound healing while reducing the infection risk<sup>37</sup>. The potential of these systems, which have the capability to inhibit microbial growth while promoting wound healing, makes them significant for application in wound healing.

Marine-derived plant extracts have been used for the creation of antimicrobial nanocomposites, which have enhanced biological activity. The creation of nanocomposites using seaweed extracts has proven to have enhanced antimicrobial and antioxidant properties.

These nanocomposites have significant inhibitory effects against bacterial pathogens, as they have the capability to cause membrane damage and oxidative stress in microorganisms<sup>38</sup>. The creation of these nanocomposites proves the potential of using marine-derived natural products for the creation of antimicrobial materials.

Another promising avenue in the fight against microbial infections is represented by metal oxide nanoparticles in a biopolymer matrix. Thus, zinc oxide nanoparticles have shown their ability to inhibit biofilm production in multidrug-resistant bacterial pathogens<sup>38</sup>. These nanoparticles interact with microbial cell membranes and produce ROS, finally causing cell death in bacteria. These nanoparticles, therefore, find their place in biomedical materials.

Natural compounds have been used in developing biodegradable packaging materials that inhibit microbial contamination in food systems. Thus, composite films based on orange peel extracts have shown their ability to inhibit microbial contamination in food systems, providing antioxidant protection at the same time. These examples demonstrate the potential use of plant-derived antimicrobial compounds in fighting microbial contamination in various fields beyond medicine. Nanocomposites play a significant role in developing antimicrobial efficacy as shown in Figure 3.

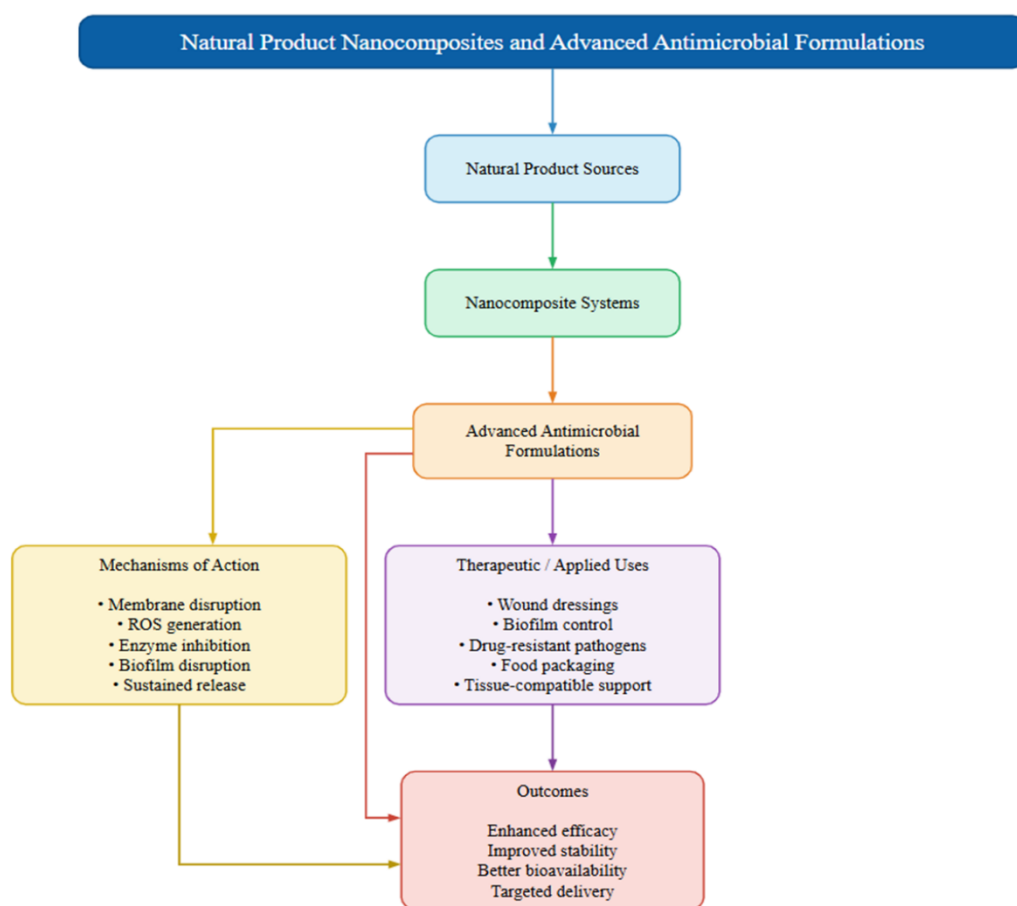


Figure 3: Natural product nanocomposites and advanced antimicrobial formulations for improved antimicrobial activity

Overall, the development of advanced antimicrobial formulations integrating natural compounds with nanotechnology and biomaterials represents a promising direction in infection control research. These systems enhance the antimicrobial properties of plant-derived compounds while enabling targeted delivery and improved therapeutic outcomes.

### 8. Plant Extracts Targeting Resistant and Foodborne Pathogens

Antimicrobial agents derived from plants have equally proven promising in the management of infections due to resistant bacterial pathogens and foodborne microorganisms. Food safety is a major concern worldwide due to the emergence and persistence of antimicrobial-resistant microorganisms in food systems<sup>39</sup>. Natural antimicrobial agents, such as those derived from plants, have the potential to replace synthetic preservatives and antibiotics in the prevention of food contamination. A variety of medicinal plants have proven bactericidal and bacteriostatic effects against clinically significant microorganisms. The bioactive compounds isolated from the fruits of *Clauseana anisata* have been found to possess significant antimicrobial effects against a variety of pathogenic microorganisms<sup>40</sup>. The bioactive compounds, such as phytosterols and furanocoumarins, inhibit the growth of microorganisms by interfering with their cellular metabolism, hence demonstrating their potential as natural antimicrobial agents.

In addition, traditional herbal formulations have been found to have antimicrobial effects against gastrointestinal infections. Some herbal formulations have been found to have inhibitory effects against the growth of *Helicobacter pylori*, a bacterium that leads to gastric ulcers and gastrointestinal infections. The herbal formulations have not only been found to inhibit the growth of bacteria but have also been seen to modulate the gut microbiota and control inflammation in the body<sup>41</sup>. Natural compounds such as *propolis* have been studied for their effects in inhibiting resistant bacterial strains. *Propolis* contains various bioactive compounds such as flavonoids and phenolic acids, which have been seen to have antimicrobial effects. The study found that *propolis* extracts can inhibit carbapenem-resistant bacteria isolated from clinical samples, which makes it possible to control antibiotic-resistant infections<sup>42</sup>. Plant extracts have also been tested for their antifungal properties against various pathogenic fungi that cause opportunistic infections. Silver nanoparticles synthesized by plant extracts have shown strong antifungal properties against multidrug-resistant *Candida* pathogens. These results show that plant-derived nanomaterials are effective against various fungal infections that are resistant to conventional antifungal drugs<sup>43</sup>.

Apart from medical applications, plant-derived antimicrobial compounds have also been tested for their application in food preservation and controlling pathogens<sup>44</sup>. Nano phytochemicals, which are synthesized using plant extracts, have shown strong inhibition of resistant food pathogens in meat products. Nano phytochemicals are plant-derived nanoparticles

that disrupt the cell membrane of microbes, thereby inhibiting the growth of bacteria<sup>45</sup>.

### 9. Conclusion

The emergence of antimicrobial resistance and the prevalence of MDR pathogens are issues of great concern. This has necessitated the search for alternative methods of therapy. The use of plant-derived compounds and naturopathic medicine has shown great promise as potential solutions to the problem of microbial resistance. This is attributed to the chemical diversity of these compounds and the complexity of their modes of action against pathogens. The phytochemical components of plants, such as phenolics, flavonoids, terpenoids, and alkaloids, are known to possess significant antimicrobial properties. The properties of these compounds allow them to target more than one pathway of microbial action, hence limiting the potential for the development of resistance. Recent developments in nanotechnology and biomaterial sciences have also increased the therapeutic efficacy of herbal antimicrobials. Green synthesis of nanoparticles and nanocomposite formulations, using herbal extracts, has shown promise for increasing the stability, bioavailability, and antimicrobial efficacy of herbal antimicrobials. In addition to human health, herbal antimicrobials also hold promise for developing novel solutions for controlling foodborne pathogens and improving food safety. Although the current research on herbal antimicrobials holds promise, some limitations and challenges exist, and future research should be directed toward mechanistic studies, developing novel technologies, and conducting rigorous human trials to establish the efficacy and safety of herbal antimicrobials as novel antimicrobial therapies. Combining traditional medicinal knowledge with conventional biomedical sciences may lead to the discovery of novel and innovative approaches to combat emerging pathogens of global health concern.

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