

## Advancement in the Use of Medicinal Plants for Therapeutic Purposes - A Review.

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### ABSTRACT

Medicinal plants have been foundational to traditional healthcare for millennia, providing accessible and cost-effective remedies. This review examines their evolving role in contemporary therapeutics, tracing progress from ancient practices to modern biomedical applications. Recent decades have witnessed a renaissance in phytotherapy driven by technological breakthroughs: green extraction using deep eutectic and supramolecular solvents, metabolic engineering via CRISPR-Cas9, and metabolomic standardization. The therapeutic efficacy of bioactive phytochemicals phenolics, flavonoids, alkaloids, glycosides, tannins, and terpenoids has been validated across antimicrobial, antioxidant, anti-inflammatory, analgesic, antidiabetic, and anticancer activities. Notably, plant compounds now function not only as direct therapeutics but also as adjuvants and resistance-modifying agents, offering novel solutions to antimicrobial resistance and viral pandemics. Innovations in nanotechnology and exosome-mediated delivery have significantly improved bioavailability and targeted administration. Despite these advances, persistent challenges in standardization, regulatory oversight, and the integration of plant and host microbiome factors remain. These are now being addressed by the emerging “phytobiome” framework, which considers plant genotype, endophytes, extraction methods, and gut microbiota as interacting determinants of efficacy. Recent regulatory approvals of plant-derived drugs and artificial intelligence-driven phytochemical discovery signal a new era of precision phytomedicine. Medicinal plants have thus transitioned from empirical remedies to dynamic, programmable tools poised to address major global health challenges in the coming decade.

**Keywords:** Medicinal plants, Phytotherapy, Bioactive compounds, Therapeutic practices, Nanotechnology, Drug discovery.

### Introduction

The use of medicinal plants for the purpose of healing has historical roots that may be traced back to ancient times. Man’s life and survival would be impossible without ‘symbiosis’ with, and extensive use of plants and plant products (Chukwuma et al., 2015). Since ages, humans have relied on nature for their basic needs for the production of foodstuff, shelters, clothing, means of transportation, fertilizers, flavors, and fragrances, and not the least, medicines (Karunamoorthi et al., 2013). A medicinal plant is any plant that in one or more of its organs contains substances that can be used for therapeutic purposes or that are precursors for the synthesis of useful drugs (Emeje et al., 2024; Krishnaprabu, 2020; Schmelzer & Gurib-Fakin, 2008).

Plants have been integral to traditional medicine systems for millennia, continuing to offer new remedies due to their accessibility, cost-effectiveness, and therapeutic efficacy (Gurib-Fakim, 2006). Recent findings indicate that numerous plant species globally are utilized for medicinal purposes, highlighting their potential for new drug development (Offor & Chinko, 2025).. Traditional medicine, distinct from scientific practices, is culturally rooted and predominantly transmitted orally (Cotton, 1996; Kong et al., 2003). In Africa, medicinal plants are crucial for addressing various illnesses, reflecting the rich cultural traditions associated with their use in indigenous communities (Emeje et al., 2024; Krishnaprabu, 2020).

The use of medicinal plants in African herbal medicine is deeply rooted in African history and culture, predating Western medicine and influenced by colonial powers (Adetunbi, 2020; Okigbo & Mmeka, 2006; Schultes, 1984). This traditional knowledge, acquired through generations, encompasses the curative properties of diverse plant components like seeds, bark, and leaves, often shared through local folklore. The preparation of herbal remedies is tailored to specific health needs, and there is potential for modern adaptation of these practices. As developed countries face challenges like synthetic drug side effects and antibiotic resistance, interest in medicinal plants is resurging, suggesting a possible integration of traditional and modern healthcare approaches (Emeze et al., 2024; Hamby, 2004; Krishnaprabu, 2020).

### **Bioactive Compounds**

Medicinal plants have been integral to human health and medicine throughout history, initially serving nutritional needs before gaining recognition for their healing properties, capable of treating various illnesses (Mustafa et al., 2017). Today, a diverse array of plant species continues to be utilized globally, particularly in Asia, South America, and Africa, for traditional therapies, highlighting the enduring significance of herbal medicine in current therapeutic practices (Bolzani et al., 2012; Durairandiyar et al., 2006; Khalid et al., 2012). Real-time population tracking indicates the global population has reached around 8.2 billion by 2025. Approximately 80% rely on traditional herbal medicine, primarily from medicinal traditions in China, India, and Africa (Alam et al., 2025; Latif & Nawaz, 2026). The WHO reports traditional medicines as the main healthcare source for 60% globally (Li & Vederas, 2009). The effectiveness of these medicines is attributed to their compatibility with the human body, cultural acceptance, and reduced side effects (Verma & Singh, 2008). Herbal medicines, increasingly adopted for various diseases, utilize over 35,000 plant species, showing a significant dependency on plant resources in traditional healthcare (Alagoz et al. 2016; Mustafa et al., 2017). The evolution of medicinal preparations from basic forms to complex formulations has led to the development of significant medications like morphine, codeine, reserpine, digoxin, vinblastine, taxol, quinine, and artemisinin, essential in current clinical practice (Latif & Nawaz, 2026).

Advanced nano-vesicular delivery methods, such as liposomes and solid lipid nanoparticles, have been developed to enhance the bioavailability and stability of herbal medicines. However, challenges related to scalability, safety, and regulatory approval persist (Saadh et al., 2024).

Bioactive compounds in plants are substances produced by plants that can have pharmacological or toxicological effects on humans and animals. They are primarily secondary metabolites, found in low amounts in foods such as fruits, vegetables, nuts, oils, and whole grains (Paulsen et al., 2010; Shrinet et al., 2021). These compounds include alkaloids, steroids, terpenoids, glycosides, saponins, tannins, phenolic compounds, and flavonoids (Agidew, 2022), which contribute to human health and exhibit various biological activities (Altemimi et al., 2017). Advances in technology have improved the characterization of these compounds, aiding in drug discovery and understanding their biosynthetic pathways (Latif & Nawaz, 2026).

### **Types of Bioactive Compounds**

Bioactive compounds, including polyphenolic compounds, carotenoids, tocopherols, phytosterols, and organosulfur compounds, are classified based on their constituents. They exhibit hydrophilic or lipophilic characteristics due to their chemical structures and are found in varying concentrations across different plant species. Their presence can be specific to certain vegetables or widespread among many plants, with fluctuations occurring in plant-based foods and the human body. Their actions against oxidative species, specificity, and complex interactions in biological systems further differentiate these compounds (Carbonell-Capella et al., 2014; Shrinet et al., 2021).

### **Natural Phenols**

Phenolics are bioactive compounds featuring an aromatic ring and hydroxyl groups, produced through metabolic pathways like the pentose phosphate, shikimate, and phenylpropanoid pathways. Present in nearly all plant parts from fruits to seeds they significantly contribute to human nutrition (Duthie et al., 2000; Shrinet et al., 2021). About half are flavonoids, pivotal in plant defense against environmental stresses (Puri & Hall, 1998) and aiding pollination (Mustafa et al., 2017).

Phenolics also function as antioxidants, antimutagens, and anticarcinogens, impacting gene expression (Marinova et al., 2005). They enhance plant coloration, with major classes including phenolic acids, flavonoids, tannins, stilbenes, and lignins, each having distinct roles in plant and human health.

### **Flavonoids**

Flavonoids, the most abundant phenolic compounds in nature, contribute color and taste to foods and play a vital role in preventing fat oxidation, thus preserving vitamins and enzymes. Common flavonoids include quercetin from onions, broccoli, and apples; catechin found in green tea; naringenin in grapefruit; and cyanidin glycoside in berries. They are classified into bioactive compounds such as anthoxanthins, anthocyanidins, flavonols/flavans/flavan-3-ols, flavanones, and isoflavonoids, each offering unique health benefits and improving food preservation (Shrinet et al., 2021; Yao et al., 2004).

### **Phenolic acid**

Phenolic acids are divided into two main subtypes: hydroxybenzoic acids and hydroxycinnamic acids. Hydroxybenzoic acids include compounds such as gallic, p-hydroxybenzoic, protocatechuic, vanillic, and syringic acids, all characterized by a C6-C1 structure. In contrast, hydroxycinnamic acids have a C6-C3 structure and include caffeic, ferulic, p-coumaric, and sinapic acids. Common sources of phenolic acids include fruits like blueberries, cranberries, and apples, as well as coffee, tea, and vegetables like spinach and lettuce. Hydroxycinnamic acids are significant contributors to phenolic bioactive compounds (Balasundram et al., 2006).

### **Alkaloids**

Alkaloids are nitrogen-containing organic bases found in a heterocyclic ring, known for their pharmacological effects. They are classified by their basic ring systems (e.g., atropine, quinoline) and plant sources (e.g., opium, vinca). Characteristically bitter and toxic, alkaloids serve as plant defenses against herbivores and pests. Their historical usage in medicinal plants is noted, especially in therapeutic roles and spiritual practices (Bruneton, 1999; Heinrich et al., 2004; van Wyk et al., 2000).

### **Glycosides**

Glycosides are secondary metabolites formed by the attachment of saccharides to an aglycone. They include groups such as cardiac glycosides, cyanogenic glycosides, glucosinolates, saponins, and anthraquinone glycosides, with flavonoids often present in glycosidic forms.

Glycosides undergo hydrolysis in the colon, releasing hydrophobic aglycones that can be absorbed into the bloodstream, highlighting their role in nutrient absorption and potential physiological effects (Paulsen et al., 2010).

### **Tannins**

Tannins are classified into two main types: condensed and hydrolysable tannins. Condensed tannins are large polymers derived from flavonoids, whereas hydrolysable tannins have a monosaccharide core, usually glucose, with attached catechin derivatives. While both types have similar properties, hydrolysable tannins are less stable and more toxic, with water solubility decreasing as the molecule size increases.

Tannins can bind to proteins and are used as astringents in treating diarrhea, skin bleedings, and transudates. They are prevalent in various plants, particularly in families such as Fagaceae and Polygonaceae, and are found in many foods and beverages, including grapes, apples, and tea (Paulsen et al., 2010; Shrinet et al., 2021).

### **Terpenoids**

Terpenoids, or isoprenoids, are the largest group of plant secondary metabolites, classified by their isoprene units into categories such as monoterpenes (C10), sesquiterpenes (C15), diterpenes (C20), triterpenes (C30), and tetraterpenes (C40). They play crucial roles in plants, including defense, thermotolerance, wound healing, and pollination, while also contributing flavors and fragrances to fruits and flowers, enhancing agricultural quality. An example is bisabolol, a sesquiterpene with medicinal properties such as antibacterial, antifungal, antimalarial, and molluscicidal effects, found in plants like *Salvia stenophylla* and *Plinia cerrocampaensis* (Heinrich et al., 2004; van Wyk et al., 2000).

## Pharmacological Actions of Bioactive Compounds in Plants

### Antimicrobial activity

A methanol extract of *P. nigrum* exhibits significant antibacterial activity against 29 Gram-negative bacterial strains, including pathogens like *P. aeruginosa* and *E. coli*, notably affecting multidrug-resistant strains. The extract's efficacy may be enhanced when combined with efflux pump inhibitors, suggesting the presence of bioactive compounds in the extract that function as such inhibitors.

Additionally, *P. nigrum* extract shows bactericidal effects against Gram-positive bacteria like *Staphylococcus aureus* (Mgbeahuruike et al., 2017). Flavonoids in garlic are implicated in reducing serious health conditions, including atherosclerosis and high cholesterol levels (Mustafa et al., 2017).

### Antioxidant properties

Antioxidants are essential food additives that improve food stability by counteracting the damaging effects of oxygen and reactive oxygen species, which can cause rancidity and color changes in food. A study by Francis & Andrew (2010) examined the antioxidant properties of *O. gratissimum* extract, finding it effectively neutralized free radicals like DPPH, demonstrating significant dose-dependent antioxidant activity comparable to ascorbic acid.

Additionally, the antioxidant effectiveness of phenolic acids correlates with the number and positioning of hydroxyl groups, with compounds like gallic acid exhibiting higher activity due to increased hydroxylation, while modifications can reduce activity, as seen in syringic acid (Shrinet et al., 2021).

### Anti-inflammatory activities

The study by Sayyah et al. (2003) found that *L. nobilis* essential oil has a strong anti-inflammatory effect, reducing paw edema in a dose-dependent manner. At 0.2 ml/kg, its efficacy matched that of piroxicam; however, *L. nobilis* effects are progressive and last over five hours, in contrast to piroxicam's diminishing effects after one hour. Continuous use of the essential oil can reduce existing inflammation, indicating its therapeutic potential.

The oil showed central depressant effects and motor impairments, likely due to eugenol and methyleugenol, which have anesthetic and muscle relaxant properties.

### Analgesic properties

The essential oil from *Laurus nobilis* demonstrates significant antinociceptive effects as shown in the tail-flick test, comparable to morphine. Its analgesic properties likely result from central nervous system effects, with key components such as  $\alpha$ -pinene,  $\beta$ -pinene, sabinene, and 4-terpineol also contributing to anti-inflammatory benefits. The oil offers antinociceptive, anti-inflammatory, and mild sedative activities, making it a viable natural alternative to traditional analgesics and NSAIDs (Sayyah et al., 2003). Additionally, alkaloids present may provide analgesic and anti-malarial effects.

### Antidiabetic properties

Diabetes mellitus, mainly type 2, is a prevalent endocrine disorder linked to significant health risks, including microvascular and macrovascular complications (Shrinet et al., 2021). The WHO forecasts that by 2025, 300 million individuals may have diabetes (Shrinet et al., 2021). This situation has spurred interest in medicinal plants as potential sources for new antidiabetic treatments, especially those with insulinomimetic properties.

Several plants have documented antidiabetic effects, such as Aloe vera, *Camellia sinensis* (green tea), and *Momordica charantia* (bitter melon), among others. These plants contain various bioactive compounds that suggest diverse mechanisms of action and warrant further investigation for their therapeutic potential (Patel et al., 2012).

### Anti-cancer activity

Cancer poses a major global health issue, causing around 10 million deaths annually with projections reaching 21 million by 2030. In 2012, the WHO reported 14.1 million new cancer cases and 8.2 million deaths, with 9.56 million premature deaths noted in 2017 (Iqbal et al., 2017; Mukherjee & Patra, 2016). Current treatment options encompass surgery, radiotherapy, chemotherapy (with harmful side effects), immunotherapy, and natural remedies (Weaver, 2014).

Approximately 40% of anticancer drugs derive from plant metabolites (Butler, 2004; Newman & Cragg, 2007); notable examples include vinca alkaloids from *Catharanthus roseus*, which disrupt microtubule functions.

Bioactive compounds such as berberine promote apoptosis (Barzegar et al., 2015), while others like capsaicin and lycopene show effectiveness in targeting various cancers through distinct molecular pathways (Almagro et al., 2015; Mustafa et al., 2017). Plant-based compounds, including indolomonoterpenic alkaloids, are emerging as promising therapeutic options against cancer and other diseases (Gaspar et al., 2014).

### **Applications in Contemporary Therapeutic Practices: Nanotechnology**

Recent advancements in the field of biomedical technology highlight the search for effective therapeutic agents linked to biodiversity (Chekol et al., 2018). Nanotechnology, which focuses on materials at the nanoscale, is being utilized across sectors such as electronics, medicine, and environmental science (Tarafdar et al., 2013). It enables the development of novel materials and targeted drug delivery systems. Nanoparticles, which can include various payload drugs and surface modifications, hold promise in various applications (Mansoori et al., 2007), with potential benefits in cancer treatment and environmental pollution reduction (Zhang et al., 2023). The field is rapidly evolving, continuously revealing new uses for nanotechnology designed to enhance societal well-being (Hull et al., 2014).

### **Cancer Therapy**

Recent advancements in cancer treatment have highlighted the potential of nanotechnology, particularly through cancer nanotechnology, which integrates science, engineering, and medicine. It facilitates early diagnosis, prevention, and tailored therapy against cancer (Misra et al., 2010). Silver nanoparticles (AgNPs) are noted for their antimicrobial properties due to their ability to generate reactive oxygen species (ROS) and induce apoptosis in cancer cells.

Research indicates that AgNPs from natural plant extracts can exhibit anti-cancer effects in lung cancer cells (Castro-Aceituno et al., 2016). Successful cancer therapies must ensure the therapeutic agents reach tumor sites effectively, minimizing harm to normal cells while promoting targeted destruction of cancer cells through controlled release mechanisms (Qin et al., 2021).

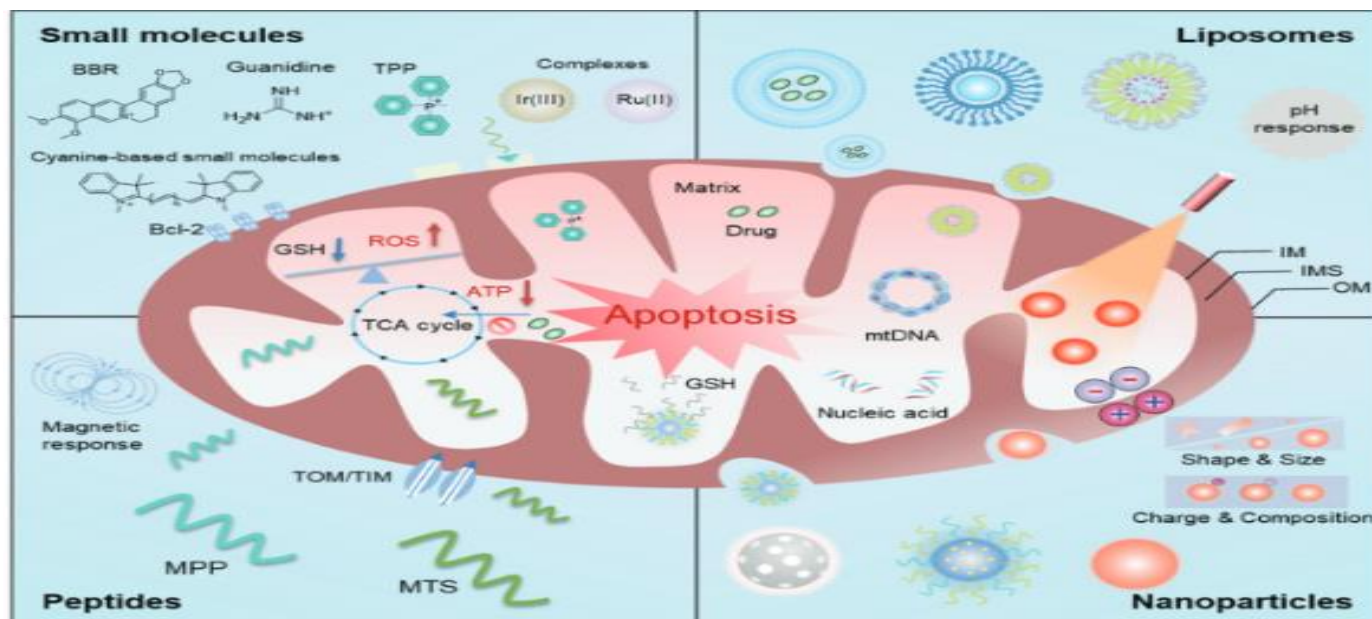
Mitochondria, double membrane-bound organelles in eukaryotic cells, play a crucial role in cell survival and metabolism by producing adenosine triphosphate (ATP), maintaining redox equilibrium, and regulating calcium levels. They also initiate apoptosis and influence cell proliferation (Qin et al., 2021). As such, they are key targets for cancer treatment, particularly through the targeted delivery of therapeutic drugs using nanotechnology. Nanoparticles, modified for improved biocompatibility and selectivity, offer promising avenues for cancer therapies by enhancing drug dispersion, optimizing drug properties, and minimizing toxicity.

Current research focuses on developing innovative mitochondria-targeting nanosystems to improve treatment efficacy compared to conventional therapies, which face challenges like toxicity and drug resistance (Qin et al., 2021).

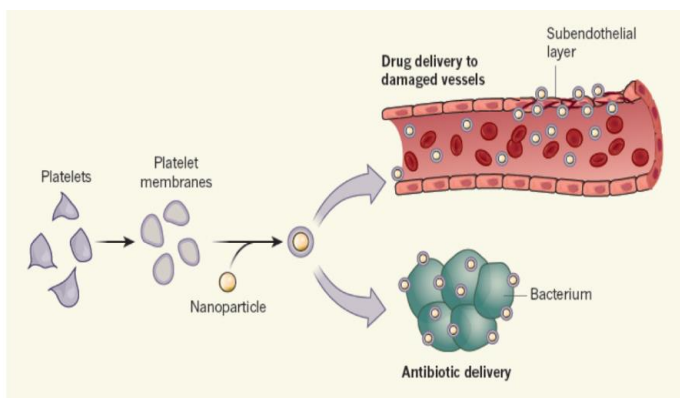
### **Antibiotics Delivery through Nanocarriers**

The increasing resistance of bacteria and fungi to current therapies presents significant challenges for healthcare professionals and government organizations globally. Traditional management approaches using high doses of oral or intravenous medications often lead to side effects and contribute to drug resistance.

To address this issue, nanotechnology is being applied. Innovative approaches involve the use of nanocarriers isolated platelet ghosts, which mimic the biological features of platelets to enhance drug delivery and evade immune detection in the body. This targeted drug release system offers benefits such as reduced dosage frequency, consistent drug effects, minimized side effects, and better control over drug levels in the body (Contera et al., 2020; Salunkhe et al., 2020).



**Fig. 1: Schematic illustration of mitochondria-targeting-based nanotechnology for cancer treatment. Construction and therapeutic strategies of mitochondria-targeted nanosystems for cancer therapy (Qin et al., 2021).**



**Fig. 2: NDDS fabrication for Infective endocarditis treatment (Hu et al., 2015).**

## Recent Progress in Harnessing Medicinal Plants for Therapeutic Uses

### Advanced Green Extraction Technologies

Recent advancements in extraction methods focus on environmentally friendly alternatives to traditional techniques. Deep eutectic solvents (DES), such as mixtures of choline chloride and glycerol (Fernández et al., 2023), have been shown to extract curcumin from *Curcuma longa* with 40% higher yield compared to 70% ethanol, while being biodegradable and recyclable.

Supramolecular solvent (SUPRAS) extraction, utilizing amphiphilic molecules, has achieved over 90% recovery of withanolides from *Withania somnifera* in a single step (Rubio et al., 2022), offering enhanced bioactivity compared to conventional methods. Additionally, ultrasound-assisted extraction (UAE) and microwave-assisted extraction (MAE) have been effectively combined with green solvents, reducing extraction times significantly, such as for flavonoids from *Ginkgo biloba*, yielding better results (Liu et al., 2024).

### Metabolic Engineering and Plant Cell Factories

Field-grown medicinal plants face challenges such as seasonal variation and low yields. To address this, Tang et al. (2021) utilized hairy root cultures from *Artemisia annua*, achieving artemisinin production comparable to field-grown plants, thereby enabling year-round production without needing agricultural land.

Additionally, Kumar et al. (2022) applied CRISPR-Cas9 technology to enhance vindoline accumulation in *Catharanthus roseus* by targeting a specific gene, which is also being explored for other medicinal compounds like paclitaxel and cannabidiol.

### **Standardization and Quality Control (Metabolomics)**

A persistent issue in phytomedicine is the variability between batches, which can be addressed through metabolomic fingerprinting with ultra-performance liquid chromatography coupled to quadrupole time-of-flight mass spectrometry (UPLC-QTOF-MS). Sharma et al. (2024) introduced a metabolomic method for a polyherbal formula involving *Berberis aristata*, *Piper nigrum*, and *Terminalia chebula*, identifying 17 marker compounds and establishing acceptable ranges ( $\pm 15\%$  relative standard deviation). This methodology is now being adopted by the Indian Pharmacopoeia Commission and the European Medicines Agency's Committee on Herbal Medicinal Products (HMPC).

### **Recent Advances in Microbiology-Related Findings**

#### ***Efflux Pump Inhibitors Reversing Antibiotic Resistance***

Efflux pumps are proteins that expel antibiotics from bacteria, notably the AcrAB-TolC system, which helps Enterobacteriaceae resist several antibiotics. Patel et al. (2022) identified that *Mentha piperita* (peppermint) oil significantly reduced the MIC of ciprofloxacin against *Salmonella enterica* serovar Typhi, while menthol and carvone were the active components. In murine models, menthol enhanced the efficacy of ciprofloxacin. Additionally, Zhao et al. (2023) showed that tannic acid from *Terminalia chebula* restored susceptibility to meropenem in carbapenem-resistant *Klebsiella pneumoniae* by inhibiting KPC-2 carbapenemase and permeabilizing the outer membrane, addressing critical treatment challenges.

#### **Anti-Biofilm Agents and Quorum Quenching**

Biofilms are resilient microbial communities resistant to antibiotics, with *Pseudomonas aeruginosa* biofilms posing significant challenges in cystic fibrosis. Research by Souza et al. (2021) demonstrated that curcumin from *Curcuma longa* reduced *P. aeruginosa* biofilm biomass by 78% at subinhibitory concentrations and inhibited virulence factor production by 90%. It also enhanced tobramycin's effectiveness considerably. Additionally, Wall et al. (2024) found that ajoene from garlic, in combination with amphotericin B, effectively eradicated *Candida albicans* biofilms, achieving significant reductions in pathogen load while disrupting the biofilm structure.

### **Gut Microbiome Modulation by Phytochemicals**

The gut microbiome plays a crucial role in metabolizing dietary compounds, leading to the production of bioactive metabolites. A study by Chen et al. (2022) demonstrated that feeding *Panax ginseng* polysaccharides to obese mice increased beneficial bacteria (*Bifidobacterium* and *Lactobacillus*) and decreased *Desulfovibrio*, correlating with improved insulin sensitivity and reduced inflammation. Additionally, research by Wang et al. (2023) on the antidiabetic effects of berberine revealed that conventional mice experienced significant blood glucose reduction, while germ-free mice did not. Metagenomic analysis found that *Clostridium* species are essential for converting berberine to a more absorbable form, leading to the development of a diagnostic tool (BerbCheck) to anticipate patient response to berberine treatment.

### **Emerging Trends in Therapeutic Utilization**

#### ***Artificial Intelligence in Phytochemical Discovery***

Sturm et al. (2024) introduced DeepPharma, a deep learning model that utilizes a graph neural network trained on 50,000 anti-mycobacterial compounds, significantly speeding up bioassay-guided fractionation from 5 years to just 9 months. This model analyzed a virtual library of 10,000 metabolites from African medicinal plants, predicting 27 compounds with potent activity. Notably, three compounds demonstrated minimum inhibitory concentrations (MIC) of 2.4, 3.1, and 4.8  $\mu\text{M}$  against *M. tuberculosis* H37Rv, while exhibiting no cytotoxicity to Vero cells.

#### ***Climate-Adapted Medicinal Plants***

Climate change alters secondary metabolite production. Liu et al. (2024) grew *Hypericum perforatum* (St. John's wort) in growth chambers at ambient (400 ppm) versus elevated (800 ppm)  $\text{CO}_2$ . Elevated  $\text{CO}_2$  increased biomass by 35% but dramatically altered phytochemical profiles: hyperforin (antidepressant) increased by 40%, while total flavonoids (quercetin, rutin, hyperoside) decreased by 30%. This is problematic because flavonoids contribute to antioxidant and anti-inflammatory effects.

The authors then tested “climate-smart” interventions: supplemental blue light (450 nm) at elevated CO<sub>2</sub> restored flavonoid levels to baseline while maintaining high hyperforin. This demonstrates that controlled environment agriculture can optimize phytochemical profiles for specific therapeutic indications.

### Regulatory Successes and Clinical Approvals

In the last decade, a total of nine plant-derived drugs received regulatory approval from the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA), or China’s National Medical Products Administration (NMPA). This represents a significant acceleration compared to the previous decade, which saw only three such approvals (ingenol mebutate from *Euphorbia peplus* for actinic keratosis, 2012; crofelemer from *Croton lechleri* for HIV-associated diarrhea; and veregen from *Camellia sinensis* for genital warts).

### Persistent Challenges

Despite regulatory progress, significant hurdles remain. These have been well documented over the last decade and continue to limit the widespread adoption of plant-based therapeutics. The challenges include:

#### *Standardization and batch-to-batch variability*

A systematic review by Gertsch (2023) of 317 randomized controlled trials on herbal medicines from 2015 to 2023 revealed that only 22% of trials reported chemical validation of extracts, which is essential for ensuring reproducibility. The majority (78%) used imprecise terminology without detailed compound specifications. A meta-analysis indicated that trials with validated extracts, such as Echinacea, demonstrated a significant effect on cold incidence, unlike those without validation. The variability in herbal content, influenced by regional and seasonal factors, further complicates standardization. Techniques like metabolomic fingerprinting exist but are often financially inaccessible for many manufacturers in low-income countries.

#### *Bioavailability and formulation costs*

The "curcumin problem" highlights the challenge of curcumin's low oral bioavailability in humans, which

is under 1% due to metabolic processing. Although phytosomes and nanoparticles can enhance bioavailability to 5-10%, they are expensive. A 2024 cost analysis revealed that a 30-day supply of silymarin phytosome costs \$240, while conventional silymarin extract costs \$15 despite being only 12% bioavailable. This situation creates a disparity where wealthier patients can afford effective phytomedicine, leaving poorer individuals with less effective options. Conversely, while andrographolide sodium bisulfite offers high solubility and bioavailability, its requirement for cold storage and intravenous administration limits its accessibility, underscoring the need for affordable oral formulations of phytochemicals.

#### *Regulatory gaps: the endophyte and microbiome blind spot*

One of the significant challenges in pharmacology is the role of the plant microbiome, where compounds often originate from endophytic fungi or bacteria rather than the plants themselves. For instance, the anticancer drug paclitaxel is produced by specific endophytes in yew trees. Surface sterilization and tissue culture can diminish a plant's ability to produce these compounds, leading to discrepancies in herbal extracts.

Current pharmacopoeias do not require testing for endophyte-derived compounds, resulting in legal issues and quality control problems. Furthermore, the host microbiome influences phytochemical activity, as seen with berberine, which relies on gut bacteria for efficacy. The lack of regulatory guidance on microbiome assessment in clinical trials contributes to failures in replicating earlier positive results in herbal medicine studies.

### Conclusion

The last decade has radically transformed medicinal plant therapeutics, evolving from crude extracts to a sophisticated, technology-driven field. Key advancements include bioactive extraction methods using biodegradable solvents, innovative formulations enhancing bioavailability, and the recognition of medicinal plants in modern clinical practice for conditions such as neuropathic pain and COVID-19.

Additionally, there has been a surge in utilizing plant compounds to combat antimicrobial resistance, employing strategies like efflux pump inhibition and quorum quenching. Data-driven discovery through AI and metabolomics has streamlined phytochemical research and personalized therapy adaptations. Future prospects involve CRISPR applications in plant genetics, synthetic phytomicrobiomes for improved efficacy, and advancements in plant-derived RNA therapeutics for direct administration. Furthermore, climate-adaptive cultivation methods will likely adapt to changing environmental conditions, ensuring consistent production of medicinal compounds. Overall, nanotechnology continues to enhance diagnostics and treatment approaches in various medical fields.

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