Current Advances in Medicinal Plant-Derived Bioactive Compounds: Phytochemistry, Pharmacological Activities, and Emerging Therapeutic Applications in Chronic Diseases. A Review

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Abstract
Medicinal plants supply an array of bioactive compounds and play an important role in addressing chronic diseases. This review describes the status of advances in several major classes of plant-based compounds: flavonoids, alkaloids, terpenoids, phenolic acids, saponins, and tannins. It specifically addresses the biosynthesis of these compounds, discusses some of the emerging pharmacological mechanisms, and presents potential therapeutic applications. The review highlights the promising effects of these classes of compounds on the treatment of cardiovascular disease, type 2 diabetes, cancer, neurodegenerative disorders, and chronic inflammation. Mechanistic and translational evidence were the focal points of the recent articles reviewed (published 2015–2025) from the databases PubMed, Scopus, and Web of Science. Current evidence suggests that many of the class compounds exert therapeutic benefits through several overlapping mechanisms that include the control of oxidative and inflammatory processes, modulation of apoptosis, regulation of glucose, and sustain endothelial function. The evidence primarily rests on *in vitro* and preclinical studies, and there are many known hurdles to the therapeutic use of these compounds (e.g., poor bioavailability, lack of standardization, multiple-compound interactions, and insufficient and underpowered clinical studies). The use of omic, artificial intelligence, and nanotechnology will aid in the development of the bioactive plant compounds clinically, but more grounded translational practices will be necessary to successfully integrate the compounds for use therapeutically in the future.

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1. Introduction

The medicinal plant field encompasses centuries of natural healing traditions, but the past decade has shown a marked increase in research into the bioactive compounds found in these plants. Interest in medicinal plants has quickly grown over the past 20 years due to their availability, cultural integration, and relative safety to synthetic pharmaceuticals [1]. The use of medicinal plants as the primary healthcare solution is reported for over 60-80% of the population in developing countries [2]. The importance of medicinal plants should be a public health focus, considering the figures reported.

The burden of managing non-communicable diseases – like diabetes, cancer, and others - have affected the capabilities of various health systems and the world over, and have spurred the need to investigate more plant-based natural compounds to gain a therapeutic service for these particular diseases [3]. The situation has also been further complicated by the emergence of various superbugs. Here too, the use of medicinal plants offers a viable solution [4].

The review is intended to provide (1) an overview of the major classes of bioactive compounds derived from medicinal plants, (2) an overview their main biosynthetic pathways, (3) an assessment of the pharmacological mechanisms along with an evaluation of the levels of evidence from *in vitro* studies, animal studies, and clinical studies, (4) an overview of the major chronic diseases and the potential role medicinal plants may have in the future, and (5) the future research opportunities and the translational and other constraints that may be currently in place.

1.1. Literature Approach

This article presents a narrative review. A targeted search of prominent scientific databases, including PubMed, Scopus, and Web of Science, was performed to find relevant literature. Preference was given to articles published between 2015 and 2025. Search terms included 'medicinal plants bioactive compounds', 'phytochemicals chronic diseases', 'plant-derived pharmacology', 'flavonoids antioxidant', 'alkaloids anticancer', and 'terpenoids anti-inflammatory'. Preference was given to peer-reviewed articles focused on the chemical classification of compounds, the molecular mechanisms of action, the bioactive compounds of plants in the treatment and management of specific diseases, the hurdles in the process of translation, and the cutting-edge research in the area. As a narrative review, the focus was on providing a general overview of the area, with a critical perspective, rather than conducting a detailed review of every piece of evidence in the area.

2. Phytochemistry: Classification and Distribution

2.1. Secondary Metabolites: Definition and Classification

Secondary metabolites are organic compounds produced by plants in reaction to specific environmental conditions, but are generally not essential for the direct cellular subsistence of the organism. These metabolites perform various functions that include defense and reproduction of the organism. There are various classes of compounds that can be chemically classified into: flavonoids, alkaloids, terpenoids, phenolic acids, saponins, and tannins. Flavonoids are the most studied compounds in the scientific literature, with over 28% of the analyzed literature [7].

2.2. Biosynthetic Pathways

Secondary metabolites are produced through three biosynthetic pathways [8]:

A. Shikimate Pathway: Starts from phosphoenolpyruvate (PEP) and erythrose 4-phosphate (E4P) leading to shikimic acid and chorismic acid, which results in the production of phenolic acids such as caffeic acid and ferulic acid. This pathway is the source of phenolic compounds, flavonoids, and lignins [9].

B. Mevalonate / MEP Pathways: Source of all terpenoids, starting from isoprene (C5) to monoterpenes like limonene and menthol, sesquiterpens, diterpens and taxol, parthenolide, triterpens and saponins such as ginsenosides and oleanolic acid [10].

C. Amino Acid Metabolism: Degradation of the amino acids, tyrosine and tryptophan (and ornithine) leads to the production of morphine, quinine, berberine, and colchicine and represents the main source of alkaloids [11].

2.3. Main Chemical Classes

Table 1*:* summarizes the structural characteristics and primary plant sources of the six major classes of bioactive compounds covered in this review [6, 7].

Class	Basic Structure	Key Examples	Notable Plant Sources
Flavonoids	C6-C3-C6 phenyl-chromanyl	Quercetin, Luteolin, Kaempferol	Onion, Apple, Green tea
Alkaloids	Heterocyclic nitrogen ring	Berberine, Morphine, Caffeine	Berberis, Poppy, Coffee
Terpenoids	Isoprene units (C5)n	Taxol, Limonene, Artemisinin	Yew tree, Citrus, Artemisia
Phenolic Acids	Benzene ring + carboxyl group	Rosmarinic, Caffeic, Chlorogenic acid	Rosemary, Coffee, Artichoke
Saponins	Triterpenoid or steroidal + sugars	Ginsenosides, Oleanolic acid	Ginseng, Licorice, Alfalfa
Tannins	Condensed or hydrolyzable polyphenol	Ellagic acid, Pomegranate tannin	Pomegranate, Acacia, Oak

3. Pharmacological Activities

3.1. Antioxidant Activity

The most well-known functional property of phenolic and flavonoid compounds is their antioxidant property [12]. These compounds have three main modes of action which are direct scavenging of free radicals, inhibition of lipid peroxidation, and induction of cellular defense enzymes such as SOD, CAT, and GPx [13]. The majority of the existing evidence is based on *in vitro* models and animal studies. It is reported that quercetin inhibits the *in vitro* oxidation of LDL-C more effectively than the well-known antioxidant vitamin E. However, studies of this type comparing quercetin and vitamin E in humans are very limited [14].

3.2. Anti-inflammatory Activity

Anti-inflammatory activity of flavonoids and terpenoids involves a multitude of mechanisms, including blocking COX-1 (and/or) COX-2 and lipoxygenase pathways, inhibiting inflammatory cytokines, TNF-α, IL-1β, IL-6, and brief modulation of NF-κB signaling pathway [3, 15]. Inflammation suppression evidence is largely derived from in vitro and animal studies where curcumin from Curcuma longa has shown prominent anti-inflammatory properties and agreeable profiles of tolerability. Comparisons of efficacy and tolerability to standard anti-inflammatory agents of curcumin in humans is virtually absent and thereby necessitates broader studies to justify the assertion of therapeutic equivalence [16].

3.3. Anticancer Activity

Several plant-derived chemical substances have exhibited cancer cell targeting potential using different pathways such as cell cycle arrest, induced apoptosis, tumor growth suppression, and created blood supply modulation through antimicrobial signaling pathways [4]. Some observations are backed by solid preliminary research, while others have already moved into clinical implications. For instance, paclitaxel, which is obtained from the Taxus species, is a helpful drug in the current field of cancer treatment [1]. On the other hand, berberine, which deactivates both the PI3K/Akt and Wnt/β-catenin pathways by targeting them in cancer cells, continues to have covalent prospects. However, it is still principally backed by mechanical data and early clinical data rather than large-scale clinical trials that are conclusive [17].

3.4. Antidiabetic Activity

Plant bioactives may carry a multitude of mechanisms to inhibit diabolic enzyme (α-glucosidase and α-amylase) and to increase AMPK pathway-mediated insulin sensitivity as well as pancreatic β cell protection from the excessive burden of reactive oxygen species (ROS) [18]. Among a few heavily analyzed cases, berberine may be put first, of which a systematic review and meta-analysis of 46 random-assign controlled investigations (RCTs) report the mean difference of total HbA1c -0.73%, the mean difference of total ± plasma FPG, and the mean difference of total insulin resistance scores expect the indices of the respective control groups [19]. However, there may be a wide variety of disparate characteristics (i.e. formulation, dose, time, quality, etc.) of each assay and/or interventions which preclude any assumption to reach a wide therapeutic equivalence across target populations considering the nuances of the study and the lack of rigor-based trials [20].

3.5. Cardiovascular Activity

Flavonoids and phenolic acids protect the cardiovascular system by preventing platelet aggregation, reducing blood pressure by inhibiting ACE enzymes, lowering LDL-C cholesterol, and increasing nitric oxide (NO) synthesis [21]. Resveratrol, found in red grapes, activates the SIRT1 protein, which aids in cardiac protection and metabolism [22]. A systematic review and meta-analysis of prospective cohort studies indicated that the consumption of six classes of flavonoids is significantly associated with a decrease in cardiovascular disease risk, with a 5% reduction in risk for every 10 mg/day increase in flavonol intake [23].

4. Therapeutic Applications in Chronic Diseases

4.1. Cardiovascular Diseases

A growing body of evidence suggests that diets rich in flavonoids and phenolic compounds may contribute to cardiovascular protection through antioxidant, anti-inflammatory, antiplatelet, and endothelial-supporting effects [21,23]. Epidemiological and observational studies indicate that higher flavonoid intake is associated with up to 20–30% lower risk of cardiovascular events [24], though causality cannot be established from such designs alone. Quercetin and myricetin have shown inhibitory effects on lipid oxidation and atherosclerotic plaque formation in experimental models, and some clinical studies document reductions in systolic blood pressure following supplementation [14]. However, despite promising experimental findings, randomized controlled trials and meta-analyses have yielded inconsistent results on the influence of these compounds on human cardiovascular parameters, warranting larger and more standardized trials [21].

4.2. Type 2 Diabetes

Because they may affect where and how glucose is absorbed in the intestines, how the liver produces glucose, how glucose and insulin interact and combine, and how quickly the body's defense to infections and other stressors wears out, many researchers have turned their focus to how medicinal plants and their phytoconstituents can help in the treatment of type 2 diabetes [18].

In literature, over 200 medicinal plants possessing blood glucose-regulating activities have been documented [2]. Fenugreek has viscous fibers which slow glucose absorption, while in other experiments, myricetin was able to inhibit hepatic glucose production [3]. In a recent Phase II, randomized clinical trial, the product of a clinical trial of the Berberine Ursodeoxycholate, HTD1801, achieved a statistically significant reduction in HbA1c levels and in fasting blood glucose levels with good tolerability [20]. Nevertheless, the absence of standard clinical guidelines for the management of diabetes using plant-based derivatives is still a concern.

4.3. Cancer

There is an expanding interest in using plant compounds as adjunct therapies and developing plant-based anticancer therapeutics due to unmet needs in oncology [4]. In preclinical studies, sulforaphane found in broccoli, stimulates Nrf2/ARE cytoprotective pathway and inhibits cancer cell growth by HDAC inhibition [17]. Ginsenosides from ginseng have demonstrated synergistic effects with certain chemotherapy agents and lessened the side effects of the treatments in some preclinical and clinical studies [1]. Most preclinical and clinical studies in humans are limited and poorly designed, and must be interpreted with caution prior to clinical implementation.

4.4. Neurodegenerative Diseases

Chronic neuroinflammation, oxidative stress, protein aggregation, and mitochondrial dysfunction are common threads in neurodegenerative disorders like Alzheimer's and Parkinson's [15]. Epigallocatechin gallate (EGCG), resveratrol, curcumin, and ginsenosides are examples of phytochemicals that have slowed beta amyloid aggregation, tau related pathology and microglial activation and have activated neuroprotective antioxidant pathways Nrf2 and SIRT1/AMPK. These phytochemicals also have the potential to enhance mitochondrial resilience and reduce dopaminergic neuronal injury in some animal models of Parkinson's [16,21]. For the most part, these phytochemicals have only been tested in animals. Although some studies have been done in humans, these studies have been of poor quality (i.e. small number of participants, poor formulation, and poor assessments) and have shown little evidence of benefit [25]. For the time being, these phytochemicals are exciting candidate therapies, especially in combination with other therapies, but ongoing research is warranted.

4.5. Arthritis and Chronic Inflammatory Diseases

Some chronic inflammatory disorders such as rheumatoid arthritis and osteoarthritis can be treated using natural compounds that have anti-inflammatory and anti-oxidant properties [3]. Multiple studies have looked into the effects of ginger extract (Zingiber officinale), curcumin, boswellic acids, and polyphenols on COX-2, NF-κB, cytokine production and oxidative damage of tissues [15,16]. Some studies have suggested that ginger and curcumin-based preparations improve symptoms especially in pain and physical activities, however, most of these studies have used different compositions and doses which have affected results of these studies [26]. Due to the tolerance and possible side effects, these compounds may be used during the management of long-term inflammation, but should not be seen as alternatives to treatments that may cause major changes in the course of the disease, especially if such treatments are indicated.

5. Modern Research and Development Technologies
5.1. Omics Technologies and Artificial Intelligence
"Omics" technologies regard the fields of genomics, proteomics, metabolomics, and spatial omics, and their combination have transformed our ability to chart the biosynthetic pathways and regulatory control networks of constituents from plants [27]. The convergence of these disciplines with Artificial Intelligence (AI) and Machine Learning (ML) is aiding the analysis of a large number of plant constituents to predict the activity of potential drug targets with a phenomenal rate of accuracy and the ability to optimize this process to a fraction of the current time [28]. These approaches can overcome the limitations in the current state of phytochemical medicine development by enabling the optimal selection and consideration of candidates for in-depth biological evaluation.

5.2. Nanotechnology-Based Drug Delivery Systems
Poor bioavailability is a major barrier to the clinical use of many plant compounds; it has been reported that the oral absorption of curcumin is less than 1% due to fast metabolism and poor solubility in water [29]. It has been reported that the use of liposomal, polymeric, and cyclodextrin-based nanoparticles within nanotechnology has the potential to facilitate a substantial increase in the bioavailability of curcumin under test conditions [30]. The review of clinical trials of curcumin formulations suggests that the use of nanotechnology in formulations of curcumin is a game changer in the bioavailability of curcumin and has a good safety profile for a number of disease indications [31]. The use of gold nanoparticles which are coated with plant polyphenols, has recently been upheld to have good theranostic potential in preclinical studies [32].

5.3. Metabolic Engineering and Biochemical Synthesis
Editing metabolic pathways in plants and microbes allows for the production of rare plant metabolites more consistently and with less cost than extracting from the field [10]. The production of artemisinin, the current leading treatment for malaria, is being done via yeast and genetic engineering to improve the availability in under-resourced locations [11]. Metabolic engineering allows for the modification of structures of compounds to improve the stability, potency, and selectivity as well as the overall decrease in side effects [8].

6. Challenges and Limitations
6.1. Standardization and Quality
The concentration of active compounds in varied plant types, influenced by different growing seasons, geographic conditions, and storage methods, may also hinder pharmaceutical standardization [6]. The WHO points out that the lack of uniform quality standards for plant extracts poses real dangers for patients and undermines the ability to design robust clinical studies [2]. Contamination by heavy metals, pesticides and microbes in herbal products, compounds the quality assurance challenge for herbal products [5].

6.2. Bioavailability and Drug Interactions
Due to first-pass metabolism and hydrophobicity, many flavonoids, such as curcumin, quercetin, and resveratrol, have been classified as poorly absorbed after oral administration [29,31]. In plant metabolites, beyond their bioavailability, they interact with drugs by clinically significant herb-drug interactions based on the inhibition or induction of hepatic CYP450 activities. Grapefruit juice metabolites, for instance, alters the plasma concentrations of anticoagulants and statins due to the inhibition of CYP3A4 [33]. In many clinical setups, these interactions are often not properly addressed, thus, a pharmacokinetic study is to be carried out to evaluate these interactions and assess the drug's efficacy [34].

6.3. The Gap from Bench to Bedside
A consistent limitation present in the literature reviewed in this article is the disproportionate amount of mechanistic evidence relative to the amount of high-quality clinical validation evidence [4, 17]. Even though there is much *in vitro* and *in vivo* evidence, there is a small number of randomized clinical trials, and those that exist are mostly inadequately powered [19, 20]. For clinical translation to be fully achieved, the safe and effective dose range of the products should be established, the complete pharmacokinetic of the products should be determined, clear molecular targets should be identified, and validated biomarkers for each of the pharmacological responses should be developed [25].

7. Future Perspectives
Several pathways can be pursued to propel the field further:

Combination therapies: that utilize plant compounds alongside standard therapies to lessen the drawbacks and optimize the convenience and efficacy of the treatments; the combination of EGCG + Taxol demonstrates anticancer synergy in preclinical studies [4].

Precision medicine: that takes into account the individual's genotype and microbiome, pharmacological response can be fine-tuned and can render a certain flavonoid that is metabolically more potent in the form of equol as is done in the case of isoflavones [27].

AI-based discovery pathways: that utilize rapid virtual screening of compound libraries to signify priority plant-based compounds to be developed as potential novel drugs [28].

Smart Nano-Encapsulation: which is based on developing stimulis responsive nanocarriers for targeted and controlled delivery of plant bioactives at disease sites [32].

The Sources of Medicinal Plants: which utilize sustainable harvesting and shielding practice paired with tissue culture and synthetic biology as a means to address the diminishing biodiversity and the threats to the environment [8].

8. Conclusions and Recommendations
This narrative review explores the scientific and therapeutic potential of plant-derived Bioactive compounds in managing chronic diseases. These compounds include flavonoids, alkaloids, terpenoids, phenolic acids, saponins, and others. These phytochemicals possess multiple biological activities and functions and target oxidative stress, inflammation, and

dysregulated metabolism, and cell proliferation and vascular dysfunction through multiple pathways. There is a clear hierarchy of evidence present in the literature. In a majority of the cases, the evidence is based primarily on cell culture and animal model-based research, while strong clinical evidence supporting the use of these phytochemicals is largely missing.

Advancements in the area of pharmacognosy will be possible only if we achieve extract standardization, optimization of pharmacokinetics, improvement of drug delivery systems, precise herb-drug interaction studies, and large randomized control trials with explicit outcomes. Innovative technologies and novel tools such as omics technologies, artificial intelligence (AI)-based advanced screening, nano-delivery systems, and metabolic engineering will enhance both the discovery and translational research. Adopting these will allow therapeutic phytochemicals to be integrated with clinical practice.

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