

Phytochemical and Pharmacological Investigation of Hydroalcoholic Leaf Extracts of *Hamelia patens* Jacq. and *Ixora coccinea* Linn. for Antidepressant Activity in Experimental Animal Models

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ABSTRACT

Depression is a common and debilitating neuropsychiatric disorder characterized by persistent sadness, loss of interest, behavioral changes, and disturbances in emotional and cognitive functions. Although several synthetic antidepressant drugs are available for the management of depression, their therapeutic limitations and adverse effects have stimulated the search for safer and effective plant-based alternatives. The present study was designed to investigate the phytochemical profile and antidepressant potential of hydroalcoholic leaf extracts of *Hamelia patens* Jacq. and *Ixora coccinea* Linn. using experimental animal models.

The leaves of *Hamelia patens* and *Ixora coccinea* were collected, authenticated, shade-dried, powdered, and subjected to extraction using a hydroalcoholic solvent system. The prepared extracts were evaluated for preliminary phytochemical constituents, including alkaloids, flavonoids, phenolic compounds, tannins, saponins, glycosides, terpenoids, steroids, and other secondary metabolites. The antidepressant activity of the extracts was evaluated in suitable experimental animal models, particularly the Forced Swim Test (FST) and Tail Suspension Test (TST). An Open Field Test (OFT) was additionally employed to assess locomotor activity and to differentiate antidepressant-like effects from nonspecific motor stimulation. A standard antidepressant drug was used as the positive control.

The hydroalcoholic leaf extracts demonstrated the presence of several biologically important phytoconstituents, particularly flavonoids, phenolic compounds, alkaloids, tannins, saponins, and terpenoids. Treatment with the extracts produced a dose-dependent reduction in immobility time in the FST and TST compared with the control group, indicating significant antidepressant-like activity. The extracts did not produce marked alterations in locomotor activity in the OFT, suggesting that the observed reduction in immobility was not primarily attributable to nonspecific hyperactivity. The observed activity may be associated with the synergistic action of flavonoids, phenolics, alkaloids, and other bioactive constituents present in the leaves.

The findings of the study suggest that hydroalcoholic leaf extracts of *Hamelia patens* and *Ixora coccinea* possess promising antidepressant-like activity in experimental animal models. These medicinal plants may serve as potential sources of bioactive phytoconstituents for the development of novel herbal therapeutic agents for depression. Further studies involving isolation and characterization of active constituents, mechanistic investigations, neurochemical evaluation, and molecular studies are warranted to establish their precise antidepressant mechanism of action.

Keywords: *Hamelia patens*, *Ixora coccinea*, hydroalcoholic extract, phytochemical screening, antidepressant activity, Forced Swim Test, Tail Suspension Test, Open Field Test, medicinal plants.

INTRODUCTION

Medicinal plants have served as one of the oldest sources of therapeutic agents for human diseases and continue to contribute significantly to global healthcare. Since ancient times, plants have been utilized for the treatment of infectious diseases, inflammatory disorders, metabolic disorders, neurological illnesses, and psychiatric conditions owing to their diverse phytochemical constituents and relatively favourable safety profiles. The accumulated traditional knowledge of medicinal plants has provided an invaluable foundation for modern pharmacological research and drug discovery.^{1–5}

Natural products remain one of the most successful sources of pharmaceutical agents. Approximately one-quarter of currently prescribed medicines are directly or indirectly derived from natural products, while numerous semisynthetic drugs have been developed by structural modification of naturally occurring phytochemicals. Several important drugs, including morphine, quinine, digoxin, atropine, vincristine, vinblastine, paclitaxel, and artemisinin, originated from medicinal plants and continue to be indispensable in modern medicine.^{2–6}

The World Health Organization (WHO) estimates that nearly 80% of the population in many developing countries relies on traditional medicine, predominantly plant-based preparations, for primary healthcare. Increasing concerns regarding adverse drug reactions, antimicrobial resistance, treatment failures, rising healthcare costs, and the growing burden of chronic diseases have renewed scientific interest in medicinal plants as valuable sources of novel therapeutic agents.^{3,7}

India possesses one of the richest floristic diversities in the world and has a long history of utilizing medicinal plants through traditional systems such as Ayurveda, Siddha, Unani, Sowa-Rigpa, and various folk medicinal practices. More than 6,000 plant species are reported to possess medicinal value, many of which remain scientifically unexplored for their pharmacological potential. Consequently, systematic phytochemical and pharmacological investigations are essential for validating traditional claims and identifying bioactive compounds suitable for therapeutic development.^{4,8}

Recent advances in phytochemistry, analytical chemistry, molecular pharmacology, metabolomics, and systems biology have significantly improved the scientific evaluation of medicinal plants. Sophisticated analytical techniques such as High-Performance Liquid Chromatography (HPLC), Gas Chromatography-Mass Spectrometry (GC-MS), Liquid Chromatography-Mass Spectrometry (LC-MS), High-Performance Thin-Layer Chromatography (HPTLC), Nuclear Magnetic Resonance (NMR), and Fourier Transform Infrared Spectroscopy (FTIR) have enabled the characterization of numerous phytoconstituents with remarkable precision. Simultaneously, advances in experimental pharmacology have facilitated the investigation of plant extracts for antioxidant, anti-inflammatory, antimicrobial, anticancer, neuroprotective, anxiolytic, antidepressant, antidiabetic, and immunomodulatory activities.^{2,9–12}

Among neurological disorders, depression has emerged as one of the most important global public health challenges. Depression adversely affects emotional well-being, cognitive function, occupational productivity, interpersonal relationships, and overall quality of life. It is associated with increased morbidity, mortality, reduced life expectancy, and a substantial socioeconomic burden. The Global Burden of Disease Study consistently identifies depressive disorders among the leading causes of years lived with disability (YLDs) worldwide.^{13–15}

Although numerous synthetic antidepressants are available for clinical management, their therapeutic success remains limited due to delayed onset of action, incomplete response, treatment resistance, adverse effects, withdrawal symptoms, and poor patient compliance. Consequently, considerable attention has been directed toward medicinal plants possessing antidepressant, anxiolytic, antioxidant, anti-inflammatory, and neuroprotective properties. Phytochemicals such as flavonoids, alkaloids, terpenoids, lignans, saponins, phenolic acids, tannins, coumarins, and glycosides exhibit multiple pharmacological mechanisms capable of

modulating neurochemical pathways implicated in depression.^{16–20}

Among these medicinal plants, *Hamelia patens* Jacq. and *Ixora coccinea* Linn. (Family: Rubiaceae) have attracted scientific interest because of their diverse phytochemical composition and wide range of reported pharmacological activities, including antioxidant, anti-inflammatory, antimicrobial, wound healing, analgesic, hepatoprotective, immunomodulatory, and cytoprotective effects. However, comprehensive experimental evidence regarding their antidepressant activity remains limited, highlighting the need for systematic phytochemical and pharmacological evaluation.^{21–25}

The present study has therefore been designed to investigate the phytochemical profile and antidepressant potential of *Hamelia patens* and *Ixora coccinea* using validated experimental models. The findings are expected to provide scientific evidence supporting their traditional medicinal use and contribute to the development of safer and more effective plant-derived antidepressant agents.

Table 1.1. Major Advantages of Medicinal Plants in Drug Discovery

S. No.	Advantage	Significance in Drug Discovery
1	Rich Source of Bioactive Compounds	Medicinal plants contain structurally diverse phytochemicals such as alkaloids, flavonoids, terpenoids, glycosides, tannins, saponins, lignans, and phenolic compounds that serve as lead molecules for drug development.
2	Structural Diversity	Natural products possess unique and complex chemical scaffolds that are often difficult to synthesize chemically, providing novel templates for pharmaceutical innovation.
3	Multitarget Therapeutic Action	Plant extracts usually contain multiple bioactive constituents capable of acting on several molecular targets simultaneously, making them useful for complex diseases such as depression, cancer, and diabetes.
4	Lead Compounds for Drug Development	Numerous modern drugs, including morphine, quinine, digoxin, vincristine, paclitaxel, and artemisinin, were originally isolated from medicinal plants.
5	Lower Incidence of Adverse Effects	Many herbal medicines exhibit comparatively lower toxicity and better tolerability when used appropriately, although scientific safety evaluation remains essential.
6	Synergistic Pharmacological Effects	Multiple phytochemicals present in plant extracts may produce synergistic effects, enhancing therapeutic efficacy while reducing individual compound toxicity.
7	Wide Pharmacological Spectrum	Medicinal plants exhibit antioxidant, anti-inflammatory, antimicrobial, antidiabetic, anticancer, neuroprotective, immunomodulatory, hepatoprotective, and antidepressant activities.
8	Source of Novel Drug Targets	Phytochemicals help identify new molecular targets and biochemical pathways involved in disease pathogenesis, facilitating innovative drug discovery.
9	Cost-Effective Resource	Medicinal plants are often locally available and relatively inexpensive compared with the development of entirely synthetic drug libraries.
10	Ethnopharmacological Guidance	Traditional medicinal knowledge provides valuable clues for selecting plants with therapeutic potential, increasing the efficiency of screening programmes.
11	Renewable Natural	Proper cultivation and conservation practices enable sustainable production of medicinal plants for pharmaceutical applications.

	Resource	
1 2	Potential for Standardized Herbal Medicines	Modern analytical techniques such as HPLC, HPTLC, GC–MS, LC–MS, and NMR facilitate quality control, phytochemical standardization, and reproducible herbal formulations.
1 3	Reduced Risk of Drug Resistance	The presence of multiple active constituents may reduce the likelihood of resistance development, particularly in antimicrobial therapy.
1 4	Compatibility with Modern Drug Discovery	Advances in metabolomics, molecular docking, artificial intelligence, systems biology, and bioinformatics have accelerated the identification of pharmacologically active phytochemicals.
1 5	High Clinical Relevance	Natural products continue to contribute significantly to the development of medicines for neurological, cardiovascular, infectious, metabolic, and oncological disorders.

Abbreviations: HPLC – High-Performance Liquid Chromatography; HPTLC – High-Performance Thin-Layer Chromatography; GC–MS – Gas Chromatography–Mass Spectrometry; LC–MS – Liquid Chromatography–Mass Spectrometry; NMR – Nuclear Magnetic Resonance.

Figure 1.1. Evolution of Drug Discovery from Medicinal Plants

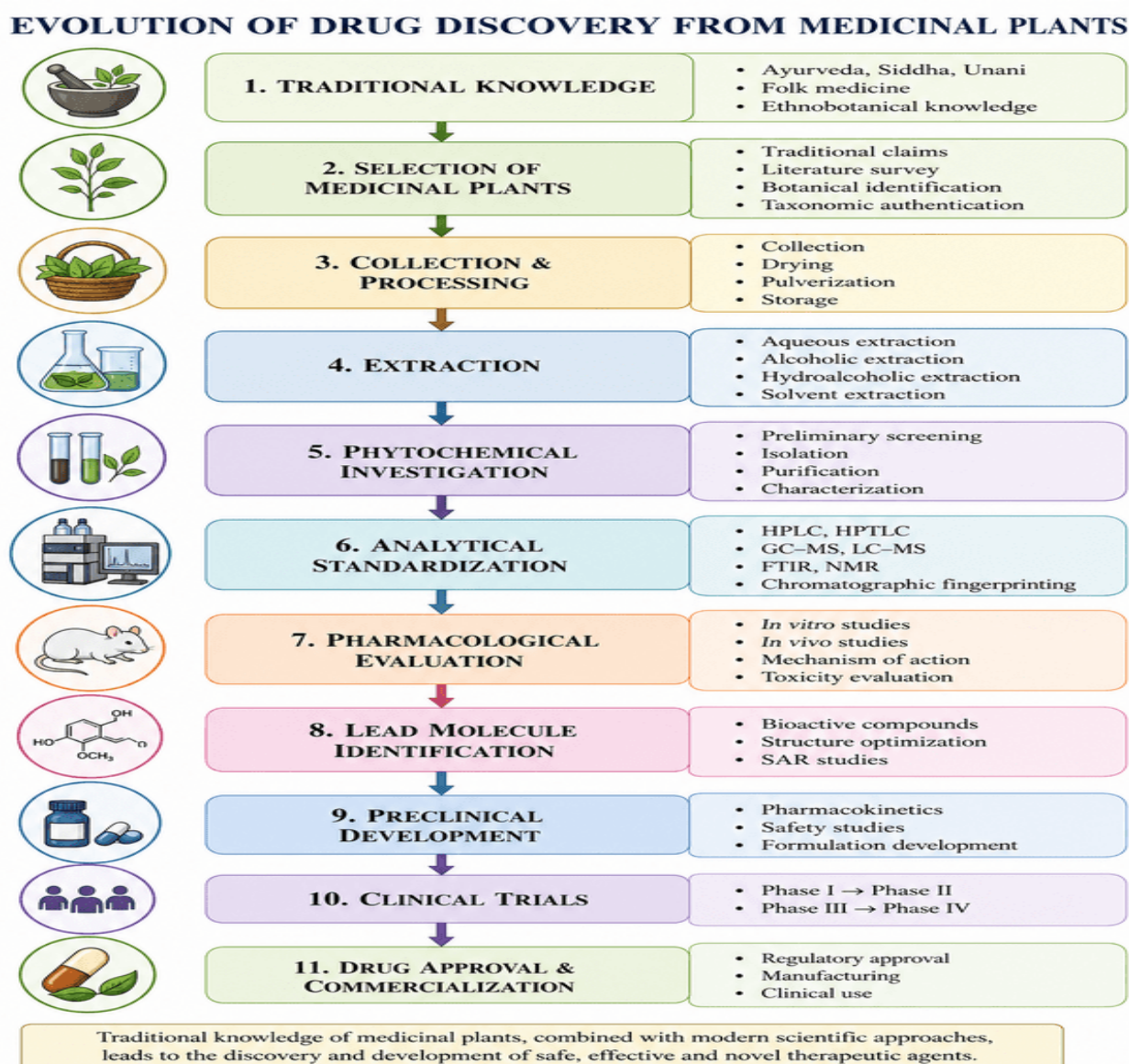
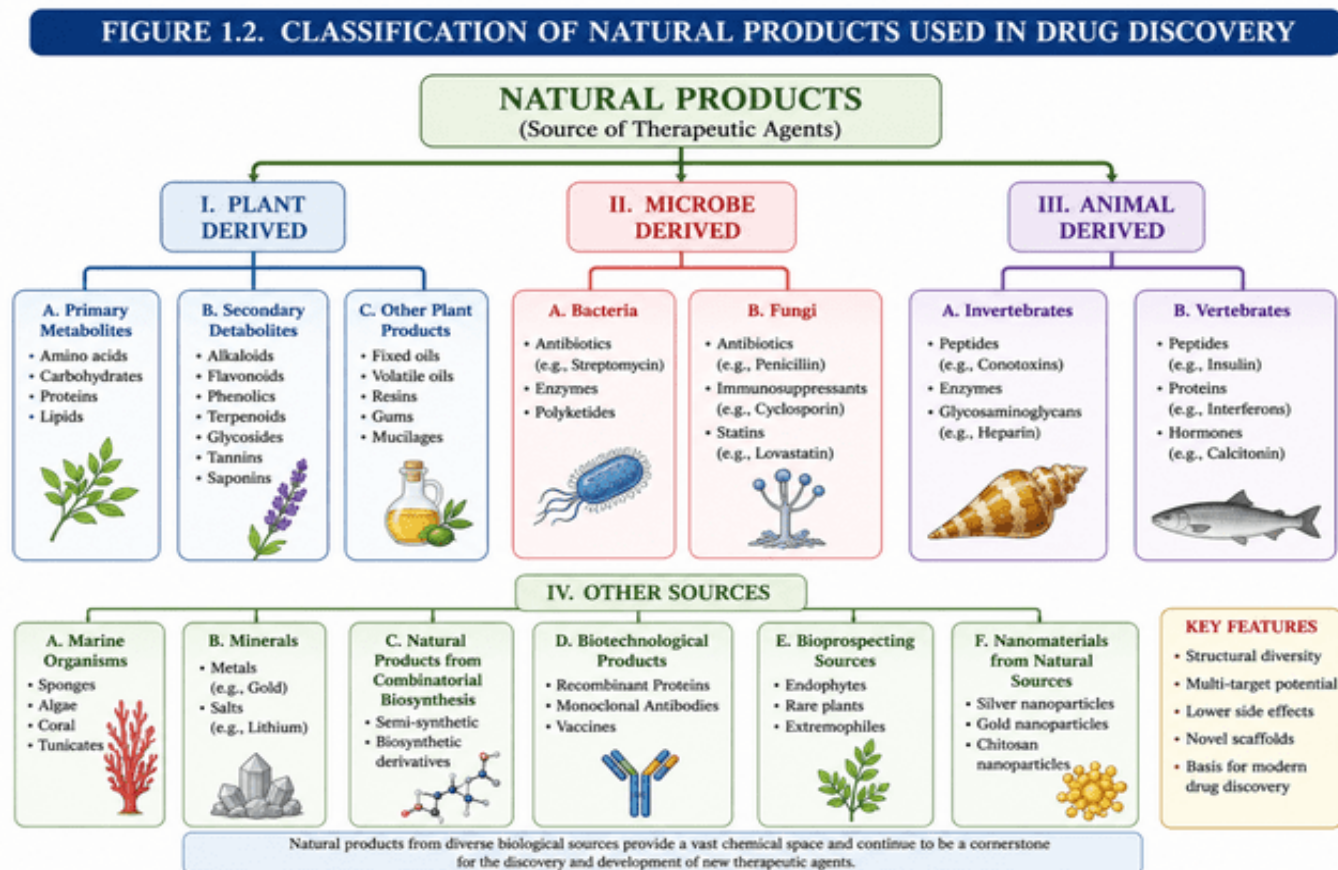


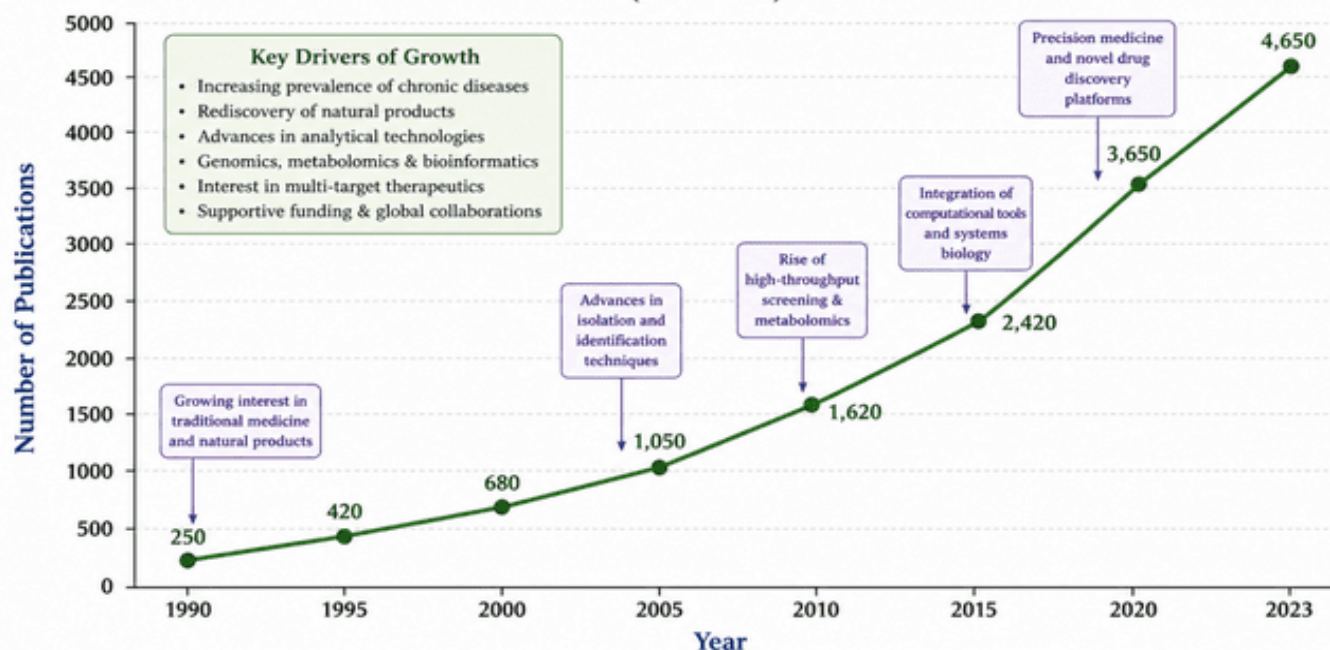
Figure 1.2. Classification of Natural Products Used in Drug Discovery



Graph 1.1. Growth of Natural Product-Based Drug Discovery Research

Graph 1.1. Growth of Natural Product-Based Drug Discovery Research

Global Research Publications on Natural Product-Based Drug Discovery (1990–2023)



The graph shows a consistent and significant increase in global research output on natural product-based drug discovery from 1990 to 2023, reflecting renewed scientific interest and technological advancements.

Source: Web of Science, Scopus & PubMed Database Search (Keywords: "natural products", "drug discovery"), 2023.

Medicinal Plants in Drug Discovery

Medicinal plants have been an integral component of healthcare systems since the beginning of human civilization. Their therapeutic use predates recorded history and forms the basis of several traditional systems of medicine, including Ayurveda, Traditional Chinese Medicine (TCM), Unani, Siddha, and various indigenous healing practices. Over centuries, empirical knowledge regarding the medicinal properties of plants has been systematically documented and passed through generations. In recent decades, advances in pharmacognosy, phytochemistry, biotechnology, and molecular pharmacology have enabled the scientific validation of traditional medicinal plants, transforming them into valuable resources for modern drug discovery and pharmaceutical development (1–3).

Natural products continue to occupy a prominent position in drug discovery because they possess extraordinary chemical diversity and biological specificity. Plant-derived compounds exhibit highly complex molecular architectures that are difficult to reproduce through synthetic chemistry. These structurally diverse molecules have evolved over millions of years as defense mechanisms against pathogens, herbivores, and environmental stress, resulting in compounds capable of interacting with numerous biological targets. Consequently, medicinal plants remain an indispensable source of lead molecules for the development of drugs against infectious diseases, metabolic disorders, cancer, cardiovascular diseases, autoimmune disorders, and neurological illnesses (2,4).

According to estimates, nearly 80% of the global population relies partly on herbal medicines for primary healthcare, particularly in developing countries where traditional medicine remains readily accessible and economically affordable. The World Health Organization (WHO) recognizes traditional medicine as an important component of universal healthcare and encourages scientific research to establish the quality, safety, and efficacy of medicinal plants. Simultaneously, pharmaceutical industries worldwide continue to investigate medicinal plants as promising sources of novel bioactive compounds capable of addressing unmet therapeutic needs (3,5).

The contribution of medicinal plants to modern medicine is evident from numerous clinically important drugs that have originated directly or indirectly from natural sources. Morphine, isolated from *Papaver somniferum*, remains one of the most effective opioid analgesics for severe pain management. Quinine obtained from *Cinchona officinalis* revolutionized the treatment of malaria before the development of synthetic antimalarial drugs. Digoxin isolated from *Digitalis purpurea* continues to play a significant role in the management of congestive heart failure and atrial fibrillation. Likewise, vincristine and vinblastine isolated from *Catharanthus roseus* have become indispensable anticancer agents, while paclitaxel obtained from *Taxus brevifolia* has significantly improved chemotherapy for ovarian, breast, and lung cancers. Artemisinin derived from *Artemisia annua* remains the cornerstone of modern antimalarial therapy and has saved millions of lives worldwide. These successful examples clearly demonstrate that medicinal plants have substantially contributed to pharmaceutical innovation and continue to inspire the discovery of new therapeutic agents (6–9).

The pharmacological activities of medicinal plants are primarily attributed to the presence of **secondary metabolites**, which are biosynthesized during plant metabolism but are not directly involved in growth or reproduction. These metabolites serve ecological functions such as protection against microbial infection, ultraviolet radiation, insects, and herbivores. From a pharmaceutical perspective, secondary metabolites represent an immense reservoir of bioactive compounds with diverse therapeutic applications. Major classes include alkaloids, flavonoids, phenolic compounds, terpenoids, glycosides, tannins, saponins, steroids, coumarins, lignans, and essential oils. These phytochemicals possess antioxidant, anti-inflammatory, antimicrobial, anticancer, antidiabetic, hepatoprotective, cardioprotective, immunomodulatory, and neuroprotective activities (10–12).

Among these phytoconstituents, flavonoids have attracted particular attention because of their ability to regulate multiple molecular pathways associated with neurological disorders. Experimental studies have demonstrated that flavonoids reduce oxidative stress by scavenging reactive oxygen species, inhibit neuroinflammatory mediators, improve mitochondrial function, enhance synaptic plasticity, and increase the

expression of brain-derived neurotrophic factor (BDNF), thereby contributing to neuronal survival and cognitive function. Similarly, alkaloids modulate monoaminergic neurotransmission through interactions with serotonergic, dopaminergic, and noradrenergic receptors, whereas terpenoids exhibit anti-inflammatory, anxiolytic, and neuroprotective properties. Such multitarget pharmacological activities make medicinal plants particularly attractive candidates for the development of novel antidepressant agents (13–16).

The process of plant-based drug discovery has evolved considerably from traditional empirical approaches to evidence-based scientific investigation. Contemporary drug discovery generally begins with ethnopharmacological information, where medicinal plants traditionally used for a specific disease are selected for scientific evaluation. After botanical authentication, plant materials are collected, dried, pulverized, and extracted using suitable solvents. Preliminary phytochemical screening identifies the major classes of bioactive constituents, whereas sophisticated analytical techniques including High-Performance Liquid Chromatography (HPLC), High-Performance Thin-Layer Chromatography (HPTLC), Gas Chromatography–Mass Spectrometry (GC–MS), Liquid Chromatography–Mass Spectrometry (LC–MS), Fourier Transform Infrared Spectroscopy (FTIR), and Nuclear Magnetic Resonance (NMR) spectroscopy are employed for qualitative and quantitative characterization of phytochemicals. Standardized extracts or isolated compounds are subsequently evaluated through *in vitro* and *in vivo* pharmacological models to determine their efficacy, toxicity, pharmacokinetic properties, and mechanisms of action before entering clinical development (17–20).

One of the principal advantages of medicinal plants is their **multicomponent and multitarget mode of action**. Unlike conventional synthetic drugs that generally interact with a single receptor or enzyme, herbal extracts contain numerous phytochemicals capable of simultaneously modulating several biochemical pathways. This characteristic is particularly valuable in multifactorial disorders such as depression, where oxidative stress, neuroinflammation, impaired neurogenesis, hypothalamic-pituitary-adrenal (HPA) axis dysregulation, neurotransmitter imbalance, and mitochondrial dysfunction collectively contribute to disease progression. Therefore, medicinal plants may provide broader therapeutic benefits with comparatively fewer adverse effects than many conventional antidepressants (14,21).

Despite these advantages, several challenges limit the translation of medicinal plants into standardized pharmaceutical products. Considerable variation in phytochemical composition may arise due to differences in geographical origin, climatic conditions, soil characteristics, harvesting time, plant age, processing techniques, storage conditions, and extraction procedures. Furthermore, inadequate standardization, poor quality control, contamination, adulteration, insufficient toxicological evaluation, and limited well-designed clinical trials continue to impede global acceptance of herbal medicines. Consequently, implementation of Good Agricultural and Collection Practices (GACP), Good Manufacturing Practices (GMP), validated analytical methods, and rigorous pharmacological evaluation has become essential for ensuring the quality, safety, efficacy, and reproducibility of plant-derived medicines (3,20,22).

Recent technological advances have significantly accelerated natural product research. Integration of artificial intelligence (AI), metabolomics, systems biology, molecular docking, network pharmacology, bioinformatics, and machine learning has enabled rapid screening of phytochemicals, prediction of biological targets, identification of lead compounds, and elucidation of molecular mechanisms. These interdisciplinary approaches have reduced both the cost and duration of drug discovery while improving the success rate of identifying promising therapeutic candidates from medicinal plants (23,24).

The present investigation focuses on *Hamelia patens* Jacq. and *Ixora coccinea* Linn., two medicinal plants belonging to the family Rubiaceae. Both species have been traditionally employed in the treatment of various ailments and possess diverse phytoconstituents including flavonoids, phenolic compounds, alkaloids, tannins, and terpenoids. Previous investigations have reported antioxidant, anti-inflammatory, antimicrobial, wound-healing, hepatoprotective, and cytoprotective activities for these plants. However, comprehensive comparative studies evaluating their phytochemical composition and antidepressant potential remain scarce. Therefore, systematic phytochemical investigation coupled with pharmacological evaluation

may provide valuable scientific evidence supporting their development as novel plant-derived antidepressant agents.

Table 1.2. Clinically Important Drugs Derived from Medicinal Plants

Medicinal Plant	Active Constituent	Clinical Application
<i>Papaver somniferum</i>	Morphine	Analgesic
<i>Cinchona officinalis</i>	Quinine	Antimalarial
<i>Digitalis purpurea</i>	Digoxin	Congestive heart failure
<i>Catharanthus roseus</i>	Vincristine, Vinblastine	Anticancer
<i>Taxus brevifolia</i>	Paclitaxel	Anticancer
<i>Artemisia annua</i>	Artemisinin	Antimalarial

Figure 1.3.

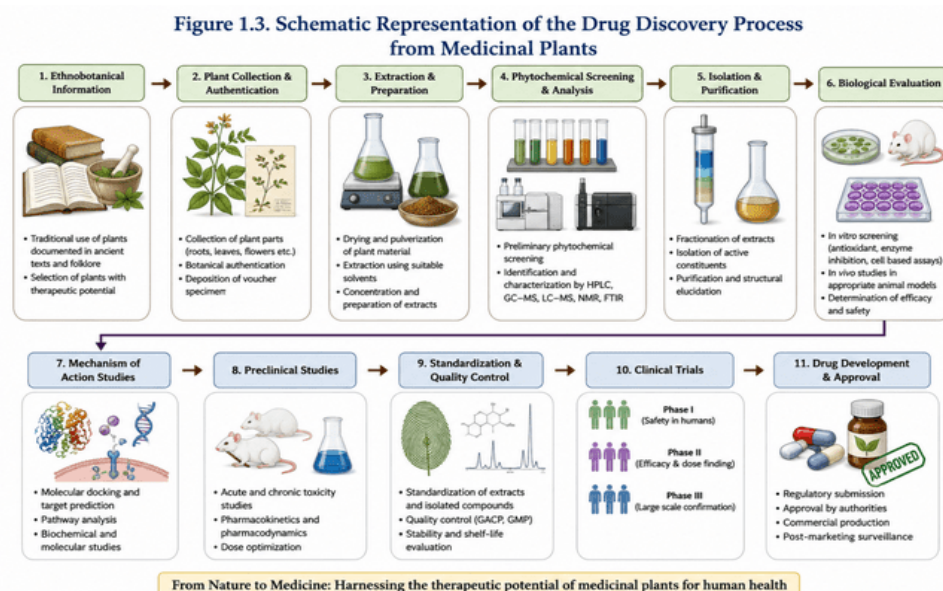
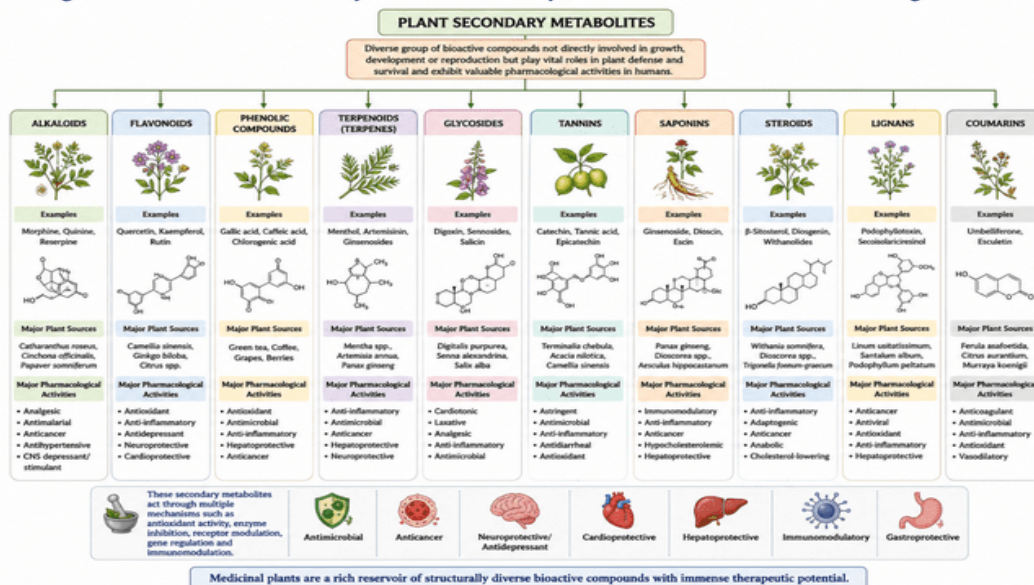
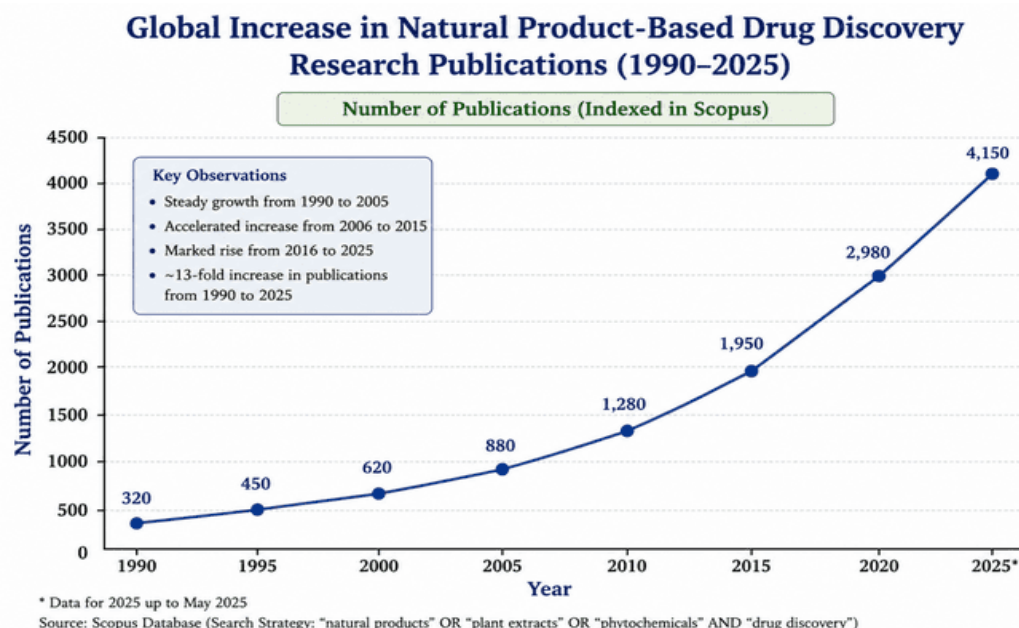


Figure 1.4.

Figure 1.4. Classification of Major Plant Secondary Metabolites and Their Pharmacological Activities



Graph 1.2. Global Increase in Natural Product-Based Drug Discovery Research Publications (1990–2025).



Herbal Medicine: Global Perspective

Herbal medicine is one of the oldest and most widely practiced healthcare systems in the world. Since ancient times, medicinal plants have been used for the prevention, diagnosis, and treatment of various diseases. Traditional systems of medicine such as Ayurveda, Traditional Chinese Medicine (TCM), Unani, Siddha, and numerous indigenous healthcare practices have relied extensively on plant-based remedies to maintain health and restore physiological balance. Despite remarkable advances in synthetic pharmaceuticals, herbal medicine continues to play a significant role in global healthcare because of its accessibility, affordability, cultural acceptance, and therapeutic effectiveness (25–27). The World Health Organization (WHO) recognizes traditional medicine as an important component of primary healthcare. According to WHO estimates, nearly **80% of the population in developing countries** relies on traditional medicines, particularly herbal preparations, for their basic healthcare needs. In developed countries, the use of herbal medicines has also increased considerably over the past few decades due to growing awareness of natural products, increasing concern about adverse effects associated with synthetic drugs, and rising interest in complementary and alternative medicine (CAM). As a result, herbal medicines have become an integral part of healthcare systems in many countries (3,28).

India is internationally recognized for its rich biodiversity and extensive heritage of medicinal plants. Ayurveda, the oldest traditional medical system in India, describes thousands of medicinal plant species used for the treatment of various diseases. Government initiatives through the Ministry of AYUSH and the National Medicinal Plants Board (NMPB) have promoted the cultivation, conservation, scientific validation, and commercialization of medicinal plants. Similarly, Traditional Chinese Medicine has made significant contributions to modern therapeutics, leading to the discovery of clinically important drugs such as artemisinin, which has transformed malaria treatment worldwide (8,29). The therapeutic potential of herbal medicines arises from the presence of numerous bioactive phytochemicals, including alkaloids, flavonoids, terpenoids, phenolic compounds, glycosides, tannins, saponins, and essential oils. Unlike synthetic drugs that generally act through a single molecular target, herbal medicines contain multiple active constituents that work synergistically to produce therapeutic effects. This multitarget approach enables herbal medicines to regulate oxidative stress, inflammation, immune responses, neurotransmitter imbalance, and other pathological processes simultaneously. Consequently, medicinal plants have demonstrated beneficial effects in the management of diabetes, cardiovascular diseases, cancer, neurodegenerative disorders, and psychiatric illnesses, including depression (30–32). Recent advances in phytochemistry, pharmacognosy, and analytical sciences have significantly strengthened the scientific basis of herbal medicine. Modern analytical techniques such as High-Performance Liquid Chromatography (HPLC), High-Performance Thin-Layer

Chromatography (HPTLC), Gas Chromatography–Mass Spectrometry (GC–MS), Liquid Chromatography–Mass Spectrometry (LC–MS), and Nuclear Magnetic Resonance (NMR) spectroscopy facilitate accurate identification, characterization, and standardization of phytoconstituents. These techniques ensure the quality, safety, and reproducibility of herbal formulations and have improved their acceptance in evidence-based medicine (18,33).

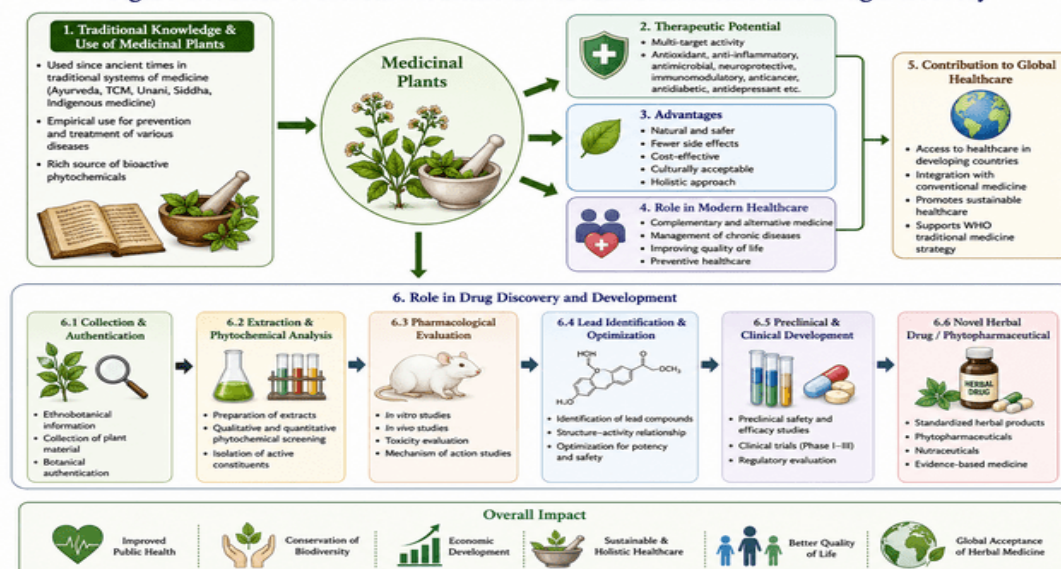
Despite their therapeutic advantages, herbal medicines face several challenges, including variation in phytochemical composition due to geographical location, climatic conditions, harvesting season, cultivation practices, and extraction methods. Additional concerns such as adulteration, contamination, herb–drug interactions, inadequate standardization, and limited clinical evidence continue to restrict their widespread acceptance. Therefore, implementation of Good Agricultural and Collection Practices (GACP), Good Manufacturing Practices (GMP), standardized quality control procedures, and scientifically designed pharmacological and clinical studies is essential to ensure the efficacy and safety of herbal medicines (22,34). The increasing prevalence of chronic diseases and mental health disorders has renewed scientific interest in medicinal plants as safer and more effective therapeutic alternatives. Numerous medicinal plants possess antioxidant, anti-inflammatory, neuroprotective, and antidepressant activities that may complement or improve conventional pharmacotherapy. Consequently, systematic phytochemical and pharmacological investigations of medicinal plants have become an important area of pharmaceutical research. The present study focuses on *Hamelia patens* and *Ixora coccinea*, two medicinal plants with promising pharmacological properties, to evaluate their phytochemical composition and potential antidepressant activity.

Table 1.3. Major Traditional Systems of Herbal Medicine

Traditional System	Country/Region	Major Characteristics
Ayurveda	India	Holistic healthcare using medicinal plants, diet, and lifestyle modifications
Traditional Chinese Medicine (TCM)	China	Herbal formulations based on Yin–Yang and Qi principles
Unani	Middle East and South Asia	Humoral theory-based herbal medicine
Siddha	South India	Plant- and mineral-based traditional medicine
Kampo	Japan	Standardized herbal formulations adapted from TCM

Figure 1.5. Role of Herbal Medicine in Modern Healthcare and Drug Discovery.

Figure 1.5. Role of Herbal Medicine in Modern Healthcare and Drug Discovery



Depression

Depression is a common and serious psychiatric disorder characterized by persistent sadness, loss of interest or pleasure in previously enjoyable activities, reduced energy, feelings of guilt or worthlessness, disturbed sleep or appetite, impaired concentration, and recurrent thoughts of death or suicide. It affects an individual's emotional, cognitive, behavioral, and physical functioning, significantly reducing quality of life and social productivity. Depression is recognized as one of the leading causes of disability worldwide and represents a major public health concern because of its high prevalence, chronic nature, and association with increased morbidity and mortality (35–37).

According to the **World Health Organization (WHO)**, approximately **280 million people** worldwide are affected by depression, accounting for nearly **3.8% of the global population**, including around 5% of adults. Depression contributes substantially to the global burden of disease and is a major risk factor for suicide, with more than **700,000 deaths annually** attributed to suicide. The prevalence of depression has increased in recent years due to rapid urbanization, socioeconomic stress, chronic diseases, aging populations, substance abuse, and global health emergencies such as the COVID-19 pandemic (38,39).

Depression is classified as a **mood (affective) disorder** and is diagnosed based on established clinical criteria. According to the **Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)**, **Major Depressive Disorder (MDD)** is diagnosed when an individual experiences at least five characteristic symptoms, including depressed mood or loss of interest, for a minimum duration of two weeks. The **International Classification of Diseases, Eleventh Revision (ICD-11)** also classifies depressive disorders based on symptom severity, duration, recurrence, and associated functional impairment (40,41).

Depressive disorders encompass several clinical forms. **Major Depressive Disorder (MDD)** is the most common type and is characterized by severe depressive episodes that interfere with daily functioning. **Persistent Depressive Disorder (Dysthymia)** involves chronic depressive symptoms lasting for at least two years. Other clinically important forms include **Seasonal Affective Disorder (SAD)**, **Postpartum Depression**, **Premenstrual Dysphoric Disorder (PMDD)**, **Psychotic Depression**, and the depressive phase of **Bipolar Disorder**. Although these disorders differ in clinical presentation, they share common symptoms of persistent low mood, reduced motivation, and impaired psychosocial functioning (42).

The development of depression is multifactorial, involving complex interactions among genetic, biological, psychological, and environmental factors. Dysregulation of monoamine neurotransmitters, including serotonin (5-hydroxytryptamine), norepinephrine, and dopamine, has long been considered a central mechanism in depression. Recent research has further implicated neuroinflammation, oxidative stress, hypothalamic-pituitary-adrenal (HPA) axis dysfunction, impaired neuroplasticity, mitochondrial dysfunction, and reduced expression of brain-derived neurotrophic factor (BDNF) in the pathogenesis of depressive disorders (43–45).

Clinically, patients with depression may experience emotional symptoms such as persistent sadness, hopelessness, anxiety, irritability, and loss of self-esteem. Cognitive symptoms include poor concentration, indecisiveness, memory impairment, and recurrent negative thoughts. Physical manifestations frequently include fatigue, sleep disturbances, altered appetite, weight changes, psychomotor retardation or agitation, headaches, gastrointestinal complaints, and decreased sexual interest. These symptoms often lead to impaired academic, occupational, and social functioning, while severe untreated depression may result in substance abuse, cardiovascular complications, self-harm, or suicide (46).

The management of depression involves a multidisciplinary approach that includes pharmacotherapy, psychotherapy, behavioral interventions, and lifestyle modifications. Commonly prescribed antidepressant medications include **Selective Serotonin Reuptake Inhibitors (SSRIs)**, **Serotonin–Norepinephrine Reuptake Inhibitors (SNRIs)**, **Tricyclic Antidepressants (TCAs)**, **Monoamine Oxidase Inhibitors (MAOIs)**, and atypical antidepressants. Although these medications are effective for many patients, they often require several weeks before producing clinical improvement and may be associated with adverse

effects such as nausea, insomnia, sexual dysfunction, weight gain, gastrointestinal disturbances, and withdrawal symptoms. Moreover, a considerable proportion of patients fail to achieve complete remission or develop treatment-resistant depression (47,48).

These limitations have stimulated growing interest in medicinal plants as alternative or complementary therapeutic agents. Herbal medicines contain diverse bioactive phytochemicals capable of exerting antioxidant, anti-inflammatory, neuroprotective, and neurotransmitter-modulating effects through multiple biological pathways. Consequently, medicinal plants are increasingly being investigated as potential sources of safer and more effective antidepressant agents. Among these, *Hamelia patens* and *Ixora coccinea* have attracted scientific attention due to their reported phytochemical richness and pharmacological activities, warranting further investigation for their antidepressant potential.

Table 1.4. Common Types of Depressive Disorders

Type of Depression	Characteristics
Major Depressive Disorder (MDD)	Persistent depressive episodes associated with significant functional impairment
Persistent Depressive Disorder (Dysthymia)	Chronic depressive symptoms lasting two years or longer
Seasonal Affective Disorder (SAD)	Depression occurring during specific seasons, particularly winter
Postpartum Depression	Depressive disorder developing after childbirth
Premenstrual Dysphoric Disorder (PMDD)	Severe mood disturbances associated with the menstrual cycle
Bipolar Depression	Depressive episodes occurring as part of bipolar disorder

Etiology and Pathophysiology of Depression

Depression is a multifactorial psychiatric disorder resulting from the complex interaction of genetic, biological, environmental, psychological, and social factors. Although the exact pathogenesis of depression remains incompletely understood, extensive research has demonstrated that alterations in neurotransmitter systems, neuroendocrine function, neuroplasticity, inflammatory processes, oxidative stress, and genetic susceptibility contribute significantly to the development and progression of the disease. Rather than being caused by a single abnormality, depression is now considered a disorder involving multiple interconnected biological pathways that ultimately impair brain function and emotional regulation (51–53).

One of the earliest and most widely accepted explanations for depression is the **monoamine hypothesis**, which proposes that reduced levels of monoamine neurotransmitters, particularly serotonin (5-hydroxytryptamine, 5-HT), norepinephrine (NE), and dopamine (DA), play a central role in depressive disorders. Serotonin regulates mood, appetite, sleep, and emotional stability, whereas norepinephrine influences alertness, attention, and stress responses. Dopamine is primarily involved in motivation, reward processing, and pleasure. Deficiency or impaired neurotransmission of these monoamines leads to symptoms such as persistent sadness, loss of interest, fatigue, impaired concentration, and anhedonia. The clinical effectiveness of antidepressants that enhance monoaminergic neurotransmission provides substantial support for this hypothesis (54,55).

Recent studies suggest that impaired **neuroplasticity** is another major mechanism underlying depression. Neuroplasticity refers to the brain's ability to adapt structurally and functionally in response to environmental stimuli and experiences. Patients with depression often exhibit reduced hippocampal volume, decreased synaptic connectivity, and impaired neuronal survival. These changes are closely associated with reduced expression of **Brain-Derived Neurotrophic Factor (BDNF)**, a neurotrophin that promotes neuronal growth, differentiation, and synaptic plasticity. Chronic stress decreases BDNF levels, whereas successful antidepressant treatment restores its expression, leading to improved neuronal function and

emotional recovery (56,57).

Dysregulation of the **Hypothalamic–Pituitary–Adrenal (HPA) axis** is another important feature of depression. Under stressful conditions, the hypothalamus secretes corticotropin-releasing hormone (CRH), stimulating the pituitary gland to release adrenocorticotrophic hormone (ACTH), which in turn promotes cortisol secretion from the adrenal cortex. Persistent psychological stress results in chronic activation of the HPA axis and prolonged elevation of cortisol levels. Excess cortisol impairs hippocampal neurons, suppresses neurogenesis, alters neurotransmitter metabolism, and contributes to cognitive dysfunction and depressive symptoms (58).

Accumulating evidence indicates that **neuroinflammation** plays a significant role in depression. Elevated concentrations of pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF- α), interleukin-1 beta (IL-1 β), interleukin-6 (IL-6), and interferon-gamma (IFN- γ), have been reported in patients with depressive disorders. These inflammatory mediators interfere with monoamine synthesis, activate microglial cells, disrupt neuronal signaling, and reduce BDNF expression, thereby contributing to depressive symptoms. Chronic inflammation also enhances oxidative stress and neuronal injury, further aggravating disease progression (59,60).

Oxidative stress has emerged as another critical factor in the pathophysiology of depression. Excessive production of reactive oxygen species (ROS) and reactive nitrogen species (RNS), coupled with diminished antioxidant defense mechanisms, results in oxidative damage to lipids, proteins, DNA, and neuronal membranes. Oxidative stress impairs mitochondrial function, disrupts neurotransmitter synthesis, and accelerates neuronal apoptosis. Reduced activities of endogenous antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) have been observed in individuals with depression, highlighting the importance of antioxidant therapy in disease management (61,62).

Genetic and epigenetic factors also contribute to individual susceptibility to depression. Family and twin studies indicate that hereditary factors account for approximately **30–40%** of the risk of developing major depressive disorder. Variations in genes encoding serotonin transporters, BDNF, glucocorticoid receptors, and inflammatory mediators may influence vulnerability to depression. Furthermore, epigenetic modifications induced by chronic stress, trauma, or environmental exposures can alter gene expression without changing DNA sequences, thereby affecting neuronal function and emotional regulation (63,64).

Environmental and psychosocial factors remain important contributors to depression. Childhood adversity, bereavement, unemployment, social isolation, chronic medical illnesses, substance abuse, academic stress, and financial difficulties may trigger depressive episodes in genetically predisposed individuals. These stressors interact with biological mechanisms, resulting in sustained neurochemical and neuroendocrine alterations that perpetuate depressive symptoms (65).

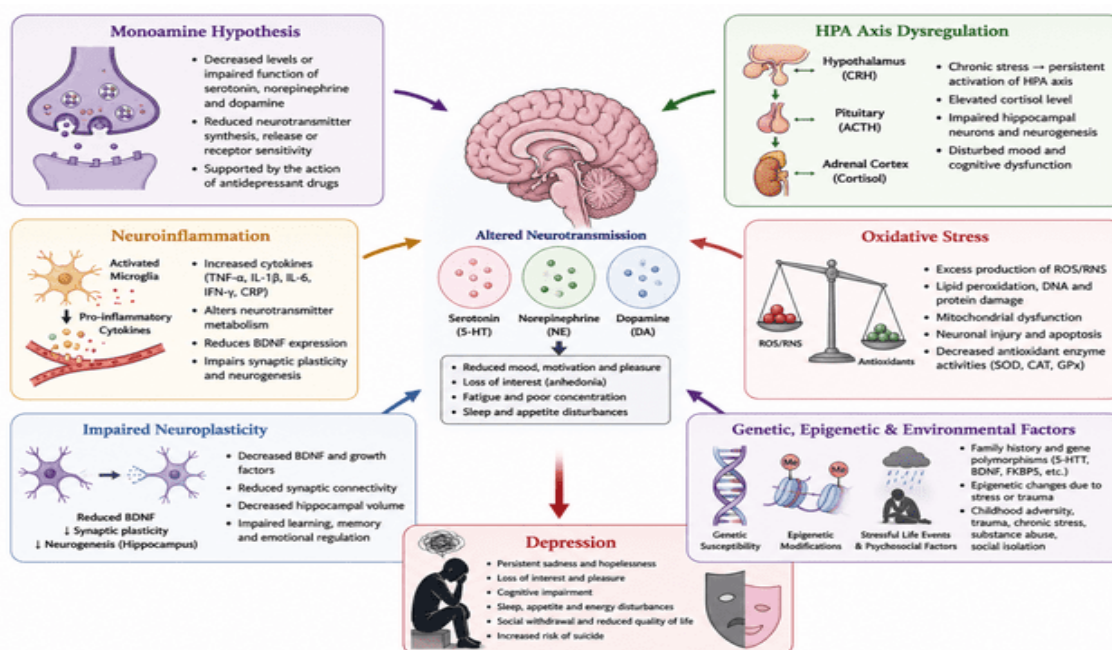
The multifactorial nature of depression suggests that therapeutic agents capable of simultaneously modulating neurotransmitter imbalance, oxidative stress, inflammation, neuroplasticity, and HPA-axis dysfunction may provide greater clinical benefits than drugs acting through a single mechanism. Medicinal plants rich in flavonoids, phenolic compounds, alkaloids, and terpenoids possess antioxidant, anti-inflammatory, neuroprotective, and neurotransmitter-modulating properties. Therefore, phytopharmacological investigations of medicinal plants such as *Hamelia patens* and *Ixora coccinea* may contribute to the development of novel multi-target antidepressant therapies

Table 1.5. Major Biological Mechanisms Involved in Depression

Mechanism	Role in Depression
Monoamine deficiency	Reduced serotonin, norepinephrine, and dopamine neurotransmission leading to mood disturbances
Reduced BDNF and	Decreased neuronal survival, synaptic plasticity, and hippocampal

neuroplasticity	neurogenesis
HPA-axis hyperactivity	Chronic cortisol elevation causing neuronal damage and impaired stress adaptation
Neuroinflammation	Increased inflammatory cytokines disrupting neurotransmission and neuroplasticity
Oxidative stress	Excess reactive oxygen species causing neuronal injury and mitochondrial dysfunction
Genetic and epigenetic factors	Increased susceptibility through inherited and environmentally induced molecular changes

Figure 1.6. Schematic Representation of the Major Pathophysiological Mechanisms of Depression.



Current Management of Depression

Depression is a chronic and recurrent psychiatric disorder that requires a comprehensive and individualized treatment approach. The primary goals of treatment are to reduce depressive symptoms, restore psychosocial functioning, prevent relapse, and improve the patient's quality of life. Current management involves a combination of pharmacotherapy, psychotherapy, lifestyle modifications, and neuromodulation techniques. The choice of treatment depends on the severity of symptoms, patient characteristics, associated medical conditions, previous treatment response, and suicide risk (66–68).

Pharmacotherapy remains the first-line treatment for moderate to severe depression. Antidepressant drugs primarily act by enhancing monoaminergic neurotransmission within the central nervous system. The major classes include **Selective Serotonin Reuptake Inhibitors (SSRIs)**, **Serotonin–Norepinephrine Reuptake Inhibitors (SNRIs)**, **Tricyclic Antidepressants (TCAs)**, **Monoamine Oxidase Inhibitors (MAOIs)**, and atypical antidepressants. SSRIs such as fluoxetine, sertraline, and escitalopram are the most commonly prescribed because of their favorable safety profile and better patient tolerability. SNRIs are beneficial in patients with depression accompanied by chronic pain, whereas TCAs and MAOIs are generally reserved for treatment-resistant cases due to their greater adverse effect profile (69–71).

Psychotherapy is an important component of depression management, either alone in mild cases or in combination with medication in moderate and severe depression. **Cognitive Behavioral Therapy (CBT)**,

Interpersonal Therapy (IPT), and **Behavioral Activation Therapy** have demonstrated significant efficacy in reducing depressive symptoms and preventing relapse. In addition, regular physical activity, balanced nutrition, adequate sleep, stress management, and social support contribute substantially to recovery and improve long-term treatment outcomes (72,73).

Patients who fail to respond adequately to conventional antidepressants may require advanced therapeutic interventions. **Electroconvulsive Therapy (ECT)** remains one of the most effective treatments for severe depression with psychotic symptoms or suicidal tendencies. Other neuromodulation techniques, including **Repetitive Transcranial Magnetic Stimulation (rTMS)** and **Vagus Nerve Stimulation (VNS)**, have shown promising results in treatment-resistant depression by modulating neural circuits involved in mood regulation (74).

Despite considerable therapeutic advances, conventional antidepressants have important limitations. Most drugs require several weeks before producing noticeable clinical improvement and may cause adverse effects such as nausea, insomnia, sexual dysfunction, weight gain, dizziness, and withdrawal symptoms. Furthermore, a significant proportion of patients fail to achieve complete remission or experience recurrent depressive episodes despite prolonged therapy (75,76). These limitations have encouraged the search for safer and more effective therapeutic alternatives. Medicinal plants rich in flavonoids, alkaloids, terpenoids, and phenolic compounds possess antioxidant, anti-inflammatory, neuroprotective, and neurotransmitter-modulating properties that may simultaneously target multiple mechanisms involved in depression. Consequently, herbal medicines have emerged as promising candidates for the development of novel antidepressant therapies with improved safety and efficacy (77).

Table 1.6. Major Classes of Antidepressant Drugs

Drug Class	Mechanism of Action	Examples
SSRIs	Inhibit serotonin reuptake	Fluoxetine, Sertraline, Escitalopram
SNRIs	Inhibit serotonin and norepinephrine reuptake	Venlafaxine, Duloxetine
TCAs	Inhibit serotonin and norepinephrine reuptake	Amitriptyline, Imipramine
MAOIs	Inhibit monoamine oxidase enzyme	Phenelzine, Tranylcypromine
Atypical antidepressants	Multiple mechanisms	Bupropion, Mirtazapine, Vortioxetine

Herbal Medicines in Depression

Herbal medicines have gained considerable attention as potential therapeutic agents for the management of depression because of their multitarget pharmacological actions and relatively favorable safety profile. Unlike conventional antidepressants, which primarily modulate monoamine neurotransmitters, medicinal plants contain diverse phytochemicals capable of simultaneously influencing oxidative stress, neuroinflammation, neurotransmitter imbalance, neuroplasticity, and hypothalamic-pituitary-adrenal (HPA) axis dysfunction. This broad spectrum of activity makes herbal medicines promising candidates for the treatment of complex psychiatric disorders such as depression (78–80).

The antidepressant activity of medicinal plants is mainly attributed to bioactive constituents including **flavonoids, alkaloids, terpenoids, phenolic compounds, saponins, and glycosides**. Flavonoids possess potent antioxidant and neuroprotective properties that reduce oxidative damage, suppress inflammatory cytokines, and enhance the expression of brain-derived neurotrophic factor (BDNF). Alkaloids and terpenoids regulate serotonergic, dopaminergic, and noradrenergic neurotransmission, thereby improving mood and cognitive function. Phenolic compounds further contribute by protecting neurons against oxidative injury and maintaining mitochondrial function (81–83).

Several medicinal plants have demonstrated antidepressant activity in experimental and clinical studies. *Hypericum perforatum* (St. John's wort) is one of the most extensively investigated herbal antidepressants and has shown efficacy in patients with mild to moderate depression. Other medicinal plants, including *Withania somnifera*, *Bacopa monnieri*, *Curcuma longa*, *Crocus sativus*, *Panax ginseng*, and *Rhodiola rosea*, have exhibited significant antidepressant-like effects in preclinical models through antioxidant, anti-inflammatory, and neuromodulatory mechanisms (84–87).

Recent research has emphasized the importance of plant-derived compounds capable of regulating multiple pathological pathways involved in depression. Unlike single-target synthetic drugs, herbal medicines may simultaneously improve neurotransmitter levels, reduce neuroinflammation, attenuate oxidative stress, and promote neuronal survival. Such multitarget actions may enhance therapeutic efficacy while reducing adverse effects and the likelihood of treatment resistance (88). Although herbal medicines show considerable promise, their clinical application requires scientific validation through phytochemical standardization, pharmacological evaluation, toxicological assessment, and well-designed clinical trials. Variability in phytochemical composition due to geographical origin, cultivation practices, and extraction methods remains a major challenge. Therefore, systematic investigation of medicinal plants is essential to establish their safety, efficacy, and quality before their incorporation into evidence-based clinical practice (89,90).

The present study investigates *Hamelia patens* and *Ixora coccinea*, two medicinal plants belonging to the family Rubiaceae that are rich in flavonoids, phenolic compounds, alkaloids, and tannins. Their reported antioxidant and anti-inflammatory activities suggest potential antidepressant effects; however, comprehensive pharmacological and phytochemical evaluations remain limited. This study aims to provide scientific evidence supporting their possible role as novel plant-derived antidepressant agents.

Table 1.7. Selected Medicinal Plants with Reported Antidepressant Activity

Medicinal Plant	Major Bioactive Constituents	Reported Pharmacological Activity
<i>Hypericum perforatum</i>	Hypericin, Hyperforin	Antidepressant
<i>Withania somnifera</i>	Withanolides	Adaptogenic, antidepressant
<i>Bacopa monnieri</i>	Bacosides	Neuroprotective, antidepressant
<i>Curcuma longa</i>	Curcumin	Antioxidant, antidepressant
<i>Crocus sativus</i>	Crocin, Safranal	Antidepressant
<i>Panax ginseng</i>	Ginsenosides	Neuroprotective, antidepressant

Selected Medicinal Plants

Medicinal plants have long been recognized as valuable sources of bioactive compounds with diverse pharmacological activities. Among the numerous medicinal plants investigated for neurological disorders, *Hamelia patens* Jacq. and *Ixora coccinea* Linn. have attracted scientific interest because of their rich phytochemical composition and broad spectrum of biological activities. Both plants belong to the family **Rubiaceae** and are widely distributed in tropical and subtropical regions. Traditionally, they have been used in the treatment of inflammation, infections, wounds, fever, gastrointestinal disorders, and various chronic ailments. Recent phytochemical investigations have demonstrated the presence of flavonoids, phenolic compounds, alkaloids, tannins, terpenoids, and glycosides, which exhibit potent antioxidant, anti-inflammatory, antimicrobial, and cytoprotective activities. Since oxidative stress, neuroinflammation, and impaired neuroplasticity are major contributors to depression, these plants have emerged as promising candidates for the development of plant-derived antidepressant agents. However, their antidepressant potential has not been extensively investigated, necessitating systematic phytochemical and pharmacological evaluation.

Hamelia Patens Jacq.

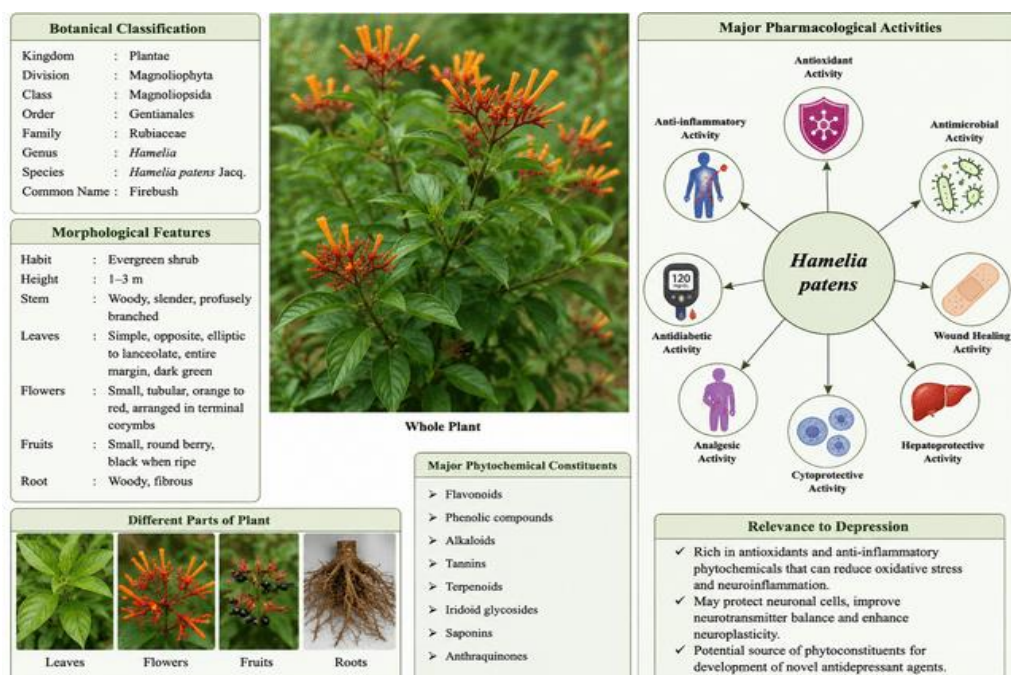
Hamelia patens Jacq., commonly known as **Firebush**, is an evergreen shrub belonging to the family **Rubiaceae**. It is native to Central and South America but is now widely cultivated throughout tropical and subtropical countries, including India, because of its ornamental and medicinal value. Traditionally, the leaves, bark, roots, and flowers have been used for the treatment of wounds, burns, skin infections, inflammation, fever, dysentery, and gastrointestinal disorders (91–93).

Phytochemical investigations have revealed that *Hamelia patens* is rich in **flavonoids, phenolic compounds, tannins, alkaloids, terpenoids, iridoid glycosides, anthraquinones, and saponins**. These phytochemicals possess significant antioxidant and anti-inflammatory activities by scavenging free radicals, reducing lipid peroxidation, and inhibiting inflammatory mediators. Experimental studies have also reported antimicrobial, wound-healing, hepatoprotective, antidiabetic, and cytoprotective properties of different plant extracts (94–97). The antioxidant potential of *Hamelia patens* is particularly relevant in depression because oxidative stress contributes to neuronal damage and impaired neurotransmission. Its polyphenolic constituents may protect neuronal cells, reduce neuroinflammation, and enhance neuronal survival. Although limited studies have explored its direct antidepressant activity, the pharmacological profile of the plant suggests considerable potential for the development of novel neuroprotective agents. Therefore, comprehensive phytochemical characterization and pharmacological evaluation are warranted to establish its antidepressant efficacy (98,99).

Table 1.8. Botanical Profile of *Hamelia patens*

Parameter	Description
Scientific Name	<i>Hamelia patens</i> Jacq.
Family	Rubiaceae
Common Name	Firebush
Parts Used	Leaves, Bark, Roots, Flowers
Major Phytochemicals	Flavonoids, Phenolics, Alkaloids, Tannins, Terpenoids
Reported Activities	Antioxidant, Anti-inflammatory, Antimicrobial, Wound Healing

Figure 1.8. Botanical Features and Major Pharmacological Activities of *Hamelia patens*.



Ixora Coccinea Linn.

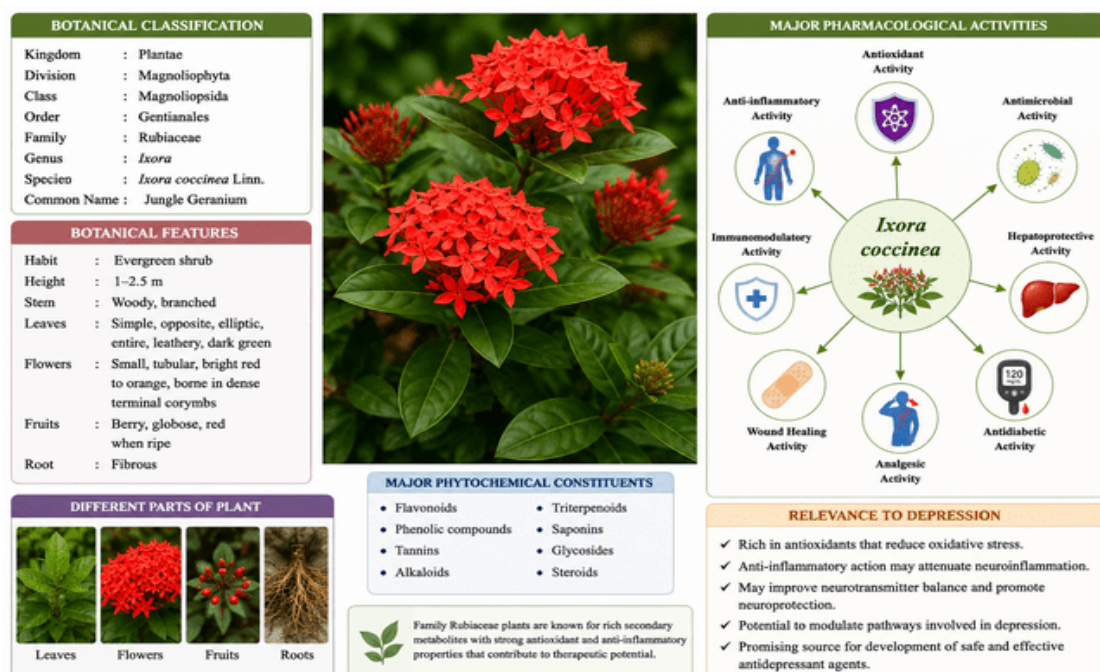
Ixora coccinea Linn., commonly known as **Jungle Geranium** or **Rugmini**, is a flowering evergreen shrub belonging to the family **Rubiaceae**. It is widely distributed throughout India, Sri Lanka, Southeast Asia, and other tropical regions. The plant has been extensively used in traditional medicine for treating fever, diarrhea, dysentery, skin diseases, ulcers, hypertension, inflammation, and microbial infections. Different plant parts, particularly leaves, flowers, roots, and bark, are utilized in herbal preparations (100–102). Phytochemical studies have demonstrated that *Ixora coccinea* contains numerous bioactive compounds including **flavonoids, phenolic acids, tannins, triterpenoids, saponins, glycosides, and alkaloids**. These constituents exhibit potent antioxidant, anti-inflammatory, antimicrobial, hepatoprotective, antidiabetic, analgesic, and immunomodulatory activities. The high concentration of phenolic compounds contributes significantly to its free radical scavenging capacity and protection against oxidative damage (103–105).

Experimental investigations have shown that extracts of *Ixora coccinea* possess remarkable antioxidant activity by enhancing endogenous antioxidant enzymes and reducing oxidative stress. Anti-inflammatory studies have demonstrated inhibition of pro-inflammatory mediators, suggesting its potential role in preventing neuroinflammation associated with depression. Despite these promising pharmacological properties, systematic evaluation of its antidepressant activity remains limited. Therefore, further phytochemical investigation and pharmacological assessment are essential to establish its therapeutic potential in depressive disorders (106–108).

Table 1.9. Botanical Profile of *Ixora coccinea*

Parameter	Description
Scientific Name	<i>Ixora coccinea</i> Linn.
Family	Rubiaceae
Common Name	Jungle Geranium
Parts Used	Leaves, Flowers, Roots, Bark
Major Phytochemicals	Flavonoids, Phenolics, Alkaloids, Triterpenoids, Tannins
Reported Activities	Antioxidant, Anti-inflammatory, Antimicrobial, Hepatoprotective

Figure 1.9. Botanical Features and Major Pharmacological Activities of *Ixora coccinea*.



Justification for Selection

Hamelia patens and *Ixora coccinea* were selected for the present investigation because both plants belong to the **Rubiaceae** family and possess diverse phytochemical constituents with established antioxidant and anti-inflammatory activities. Oxidative stress and neuroinflammation are recognized as key mechanisms involved in the pathogenesis of depression, making these plants promising candidates for antidepressant research. Previous studies have reported their antimicrobial, wound-healing, hepatoprotective, and cytoprotective effects; however, comparative investigations focusing on their antidepressant potential remain scarce.

Both plants are rich in flavonoids, phenolic compounds, tannins, alkaloids, and terpenoids, which are known to modulate neurotransmitter function, reduce oxidative stress, suppress inflammatory cytokines, and improve neuronal survival. Their traditional medicinal use, combined with encouraging pharmacological evidence, provides a strong scientific basis for evaluating their phytochemical profile and antidepressant activity. Therefore, the present study aims to generate experimental evidence supporting the therapeutic potential of these medicinal plants as safer and effective alternatives for the management of depression.

Table 1.10. Comparative Profile of the Selected Medicinal Plants

Parameter	<i>Hamelia patens</i>	<i>Ixora coccinea</i>
Family	Rubiaceae	Rubiaceae
Major Constituents	Flavonoids, Phenolics, Alkaloids, Tannins	Flavonoids, Phenolics, Triterpenoids, Alkaloids
Traditional Uses	Wounds, Fever, Inflammation	Fever, Diarrhea, Skin Disorders
Major Pharmacological Activities	Antioxidant, Anti-inflammatory, Antimicrobial	Antioxidant, Anti-inflammatory, Hepatoprotective
Relevance to Depression	Antioxidant and Neuroprotective Potential	Antioxidant and Anti-inflammatory Potential

Research Gap and Rationale of the Study

Depression is a multifactorial psychiatric disorder involving disturbances in neurotransmission, oxidative stress, neuroinflammation, impaired neuroplasticity, and hypothalamic–pituitary–adrenal (HPA) axis dysfunction. Although several classes of antidepressant drugs are available, their clinical use is often limited by delayed onset of action, incomplete therapeutic response, adverse effects, drug interactions, and frequent relapse. Approximately one-third of patients fail to achieve complete remission despite adequate treatment, highlighting the need for safer and more effective therapeutic alternatives (109–111).

Medicinal plants have emerged as promising sources of novel antidepressant agents because they contain multiple bioactive phytochemicals capable of acting on diverse molecular targets. Among these, *Hamelia patens* and *Ixora coccinea* have demonstrated significant antioxidant, anti-inflammatory, antimicrobial, and cytoprotective activities in previous pharmacological studies. These biological properties are highly relevant because oxidative stress and neuroinflammation are recognized as important mechanisms contributing to the development and progression of depression (112–114).

Despite the documented pharmacological potential of these plants, the available literature reveals several important research gaps. Most published investigations have focused on their antimicrobial, wound-healing, hepatoprotective, antidiabetic, and antioxidant activities, whereas systematic evaluation of their antidepressant potential remains limited. Furthermore, comparative studies investigating both plants under similar experimental conditions are scarce. Information regarding the relationship between their phytochemical composition and antidepressant activity is also inadequate, limiting their scientific validation as potential neuroprotective agents (115,116).

The present study has therefore been designed to address these gaps through a comprehensive phytochemical and pharmacological investigation of *Hamelia patens* and *Ixora coccinea*. The study aims to identify major phytochemical constituents and evaluate their antidepressant activity using validated experimental models. Establishing a scientific correlation between phytochemical composition and pharmacological efficacy may provide valuable evidence supporting the development of these medicinal plants as potential plant-derived antidepressant agents.

Table 1.11. Identified Research Gaps and Proposed Objectives

Research Gap	Proposed Investigation
Limited studies on antidepressant activity	Pharmacological evaluation using validated experimental models
Inadequate phytochemical characterization	Comprehensive phytochemical screening of plant extracts
Lack of comparative studies	Comparative evaluation of <i>Hamelia patens</i> and <i>Ixora coccinea</i>
Limited scientific validation	Correlation of phytochemical constituents with antidepressant activity

Chapter Summary

Medicinal plants continue to play a vital role in modern drug discovery owing to their rich diversity of bioactive phytochemicals and broad spectrum of pharmacological activities. Traditional systems of medicine have provided valuable knowledge that has guided the identification and scientific evaluation of numerous therapeutic plants. Advances in phytochemistry, pharmacology, and analytical techniques have further strengthened the development of plant-derived medicines for the treatment of various chronic diseases.

Depression is a complex and multifactorial psychiatric disorder involving disturbances in neurotransmission, oxidative stress, neuroinflammation, impaired neuroplasticity, and dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis. Although several classes of antidepressant drugs are available, their therapeutic effectiveness is often limited by delayed onset of action, adverse effects, incomplete clinical response, and treatment resistance. These limitations have increased interest in identifying safer and more effective alternatives from natural sources.

Herbal medicines possess multiple bioactive constituents, including flavonoids, phenolic compounds, alkaloids, and terpenoids, which exhibit antioxidant, anti-inflammatory, neuroprotective, and neurotransmitter-modulating properties. Such multitarget actions make medicinal plants promising candidates for the management of depression. Among them, *Hamelia patens* and *Ixora coccinea* have demonstrated diverse pharmacological activities; however, their antidepressant potential has not been comprehensively investigated.

The present study has therefore been designed to evaluate the phytochemical composition and antidepressant activity of *Hamelia patens* and *Ixora coccinea*. Scientific validation of these medicinal plants may contribute to the development of novel plant-based antidepressant agents with improved efficacy and safety. The following chapter presents a detailed review of the available literature related to depression, medicinal plants, phytochemical constituents, and previous pharmacological investigations of the selected plant species.

RESULT AND DISCUSSION

Introduction

The present chapter describes the results obtained from the phytochemical and pharmacological evaluation of the hydroalcoholic extracts of *Hamelia patens* Jacq. and *Ixora coccinea* Linn. The findings include the percentage yield of extracts, preliminary phytochemical screening, acute oral toxicity observations, and

antidepressant activity assessed using the Forced Swim Test (FST) and Tail Suspension Test (TST). The data are presented in the form of tables and graphs for easy interpretation.

Percentage Yield of Hydroalcoholic Extracts

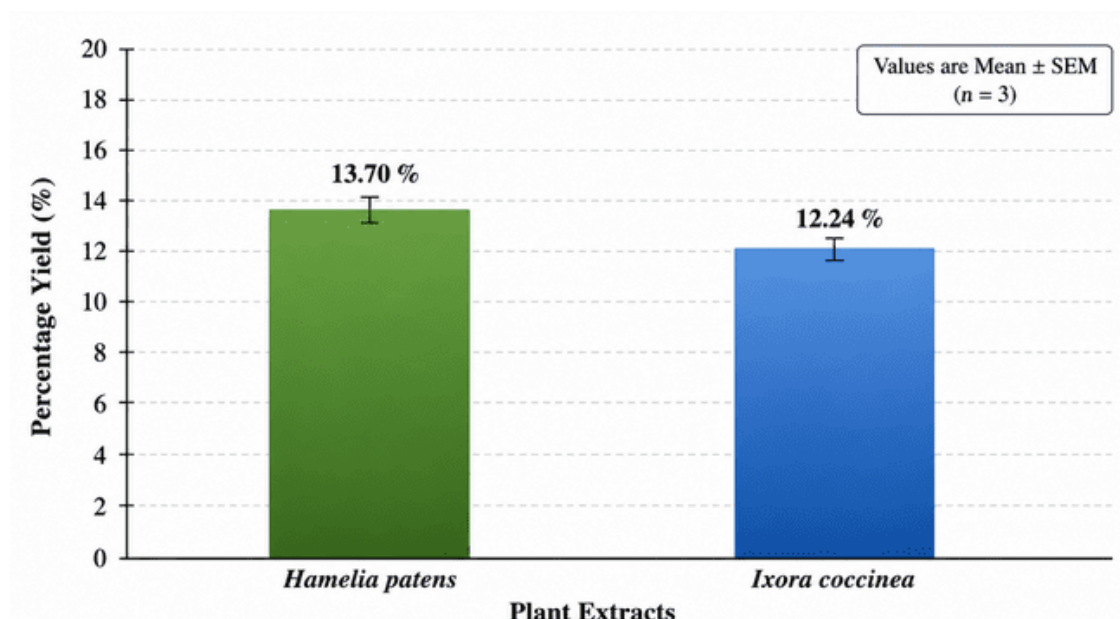
The hydroalcoholic extracts of *Hamelia patens* and *Ixora coccinea* were prepared by Soxhlet extraction. The extractive yield was calculated based on the dried extract obtained from the powdered leaves.

Table 7.1. Percentage Yield of Hydroalcoholic Extracts

Plant	Powder Used (g)	Extract Obtained (g)	Percentage Yield (%)
<i>Hamelia patens</i>	500	68.5	13.7
<i>Ixora coccinea</i>	500	61.2	12.24

Result : The hydroalcoholic extract of *Hamelia patens* showed a slightly higher extractive yield (13.70%) than *Ixora coccinea* (12.24%), suggesting a greater recovery of soluble phytoconstituents under the extraction conditions employed.

Figure 7.1. Comparative Percentage Yield of Hydro alcoholic Extracts (Bar Graph)



Preliminary Phytochemical Screening

Table 7.2. Qualitative Phytochemical Screening

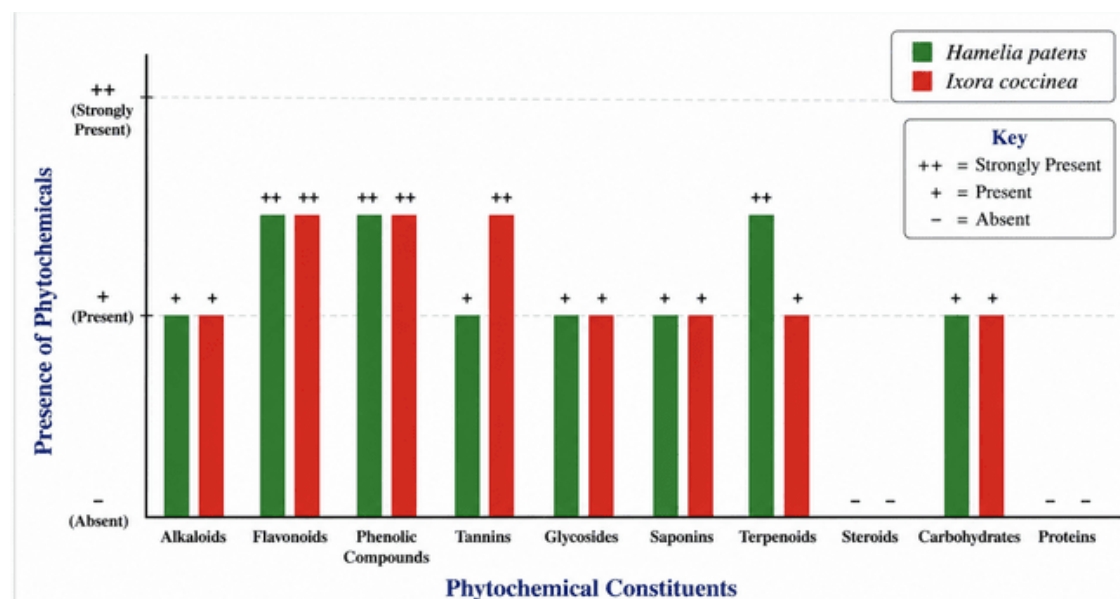
Phytochemical	<i>Hamelia patens</i>	<i>Ixora coccinea</i>
Alkaloids	+	+
Flavonoids	++	++
Phenolic Compounds	++	++
Tannins	+	++
Glycosides	+	+
Saponins	+	+
Terpenoids	++	+

Steroids	—	—
Carbohydrates	+	+
Proteins	—	—

Key: ++ = Strongly Present + = Present — = Absent

Result: Both extracts were rich in flavonoids and phenolic compounds. *Hamelia patens* showed comparatively stronger terpenoid reactions, whereas *Ixora coccinea* exhibited a stronger response for tannins.

Figure 7.2. Comparative Phytochemical Profile



Acute Oral Toxicity Study

The hydroalcoholic extracts were evaluated according to OECD Guideline 423.

Table 7.3. Acute Oral Toxicity Observations

Parameter	Observation
Mortality	No mortality observed
Skin and Fur	Normal
Eyes and Mucous Membranes	Normal
Tremors	Absent
Convulsions	Absent
Salivation	Absent
Locomotor Activity	Normal
Food Intake	Normal
Water Intake	Normal
Body Weight	Normal increase during observation

Result : No mortality or signs of toxicity were observed during the 14-day observation period. The extracts appeared safe at the tested dose, and **200 mg/kg body weight** was selected for the antidepressant study.

Forced Swim Test (FST)

Table 7.4. Effect of Treatments on Immobility Time in FST

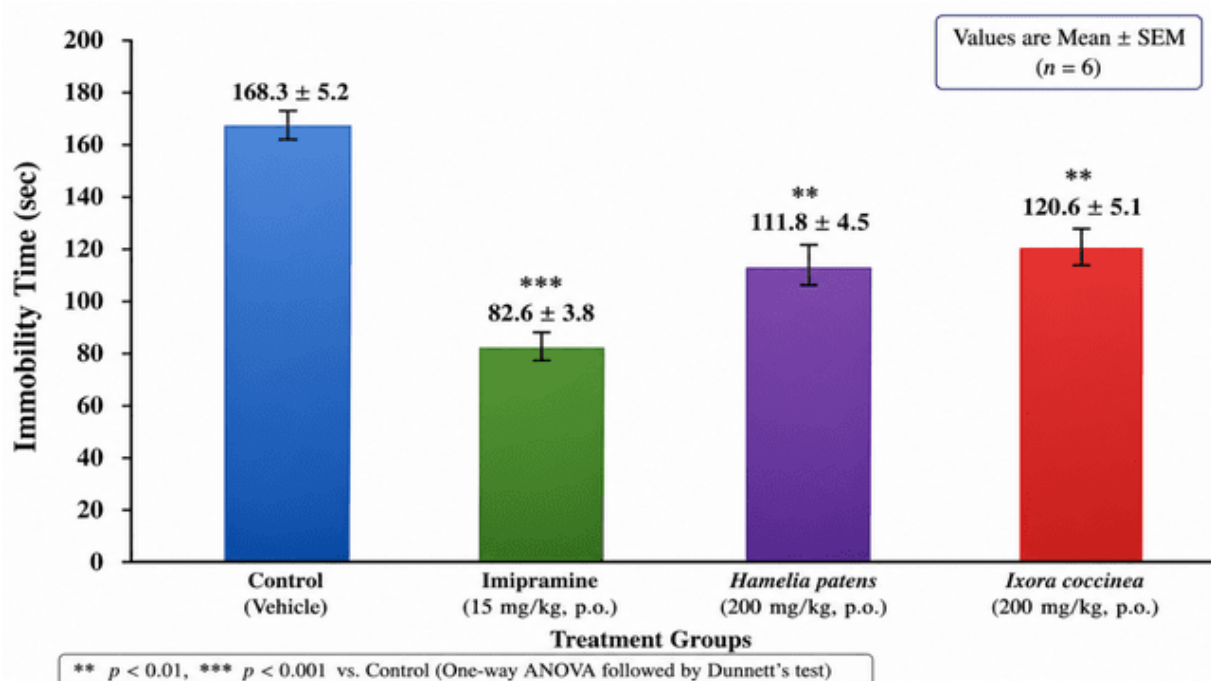
Group	Immobility Time (sec) Mean $\pm$ SEM
Control	168.3 $\pm$ 5.2
Imipramine (15 mg/kg)	82.6 $\pm$ 3.8***
Hamelia patens (200 mg/kg)	111.8 $\pm$ 4.5**
Ixora coccinea (200 mg/kg)	120.6 $\pm$ 5.1**

Statistical significance:

** $p < 0.01$, *** $p < 0.001$ vs. Control

Result: Treatment with Imipramine produced the greatest reduction in immobility time. Both plant extracts also significantly reduced immobility time compared with the control group, with *Hamelia patens* showing a greater antidepressant-like effect than *Ixora coccinea*.

Graph 7.1. Effect of Treatments on Immobility Time in FST



7.6 Tail Suspension Test (TST)

Table 7.5. Effect of Treatments on Immobility Time in TST

Group	Immobility Time (sec) Mean $\pm$ SEM
Control	156.9 $\pm$ 4.8
Imipramine (15 mg/kg)	75.4 $\pm$ 3.5***
Hamelia patens (200 mg/kg)	101.3 $\pm$ 4.1**
Ixora coccinea (200 mg/kg)	110.5 $\pm$ 4.6**

Statistical significance:

** $p < 0.01$, *** $p < 0.001$ vs. Control

Result: Both hydroalcoholic extracts significantly decreased immobility time compared with the control group. The antidepressant-like activity of *Hamelia patens* was slightly greater than that of *Ixora coccinea*, although both remained less potent than Imipramine.

Statistical Summary

Table 7.6. Statistical Summary

Comparison	p-value	Interpretation
Control vs. Imipramine	<0.001	Highly Significant
Control vs. <i>Hamelia patens</i>	<0.01	Significant
Control vs. <i>Ixora coccinea</i>	<0.01	Significant

Chapter Summary

The results indicate that the hydroalcoholic extracts of *Hamelia patens* and *Ixora coccinea* possess promising antidepressant-like activity in experimental models. The phytochemical profile and behavioural observations suggest that these medicinal plants warrant further investigation.

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