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Therapeutic Role of Medicinal Plants in Combating Air Pollution-Induced Inflammation and Anxiety

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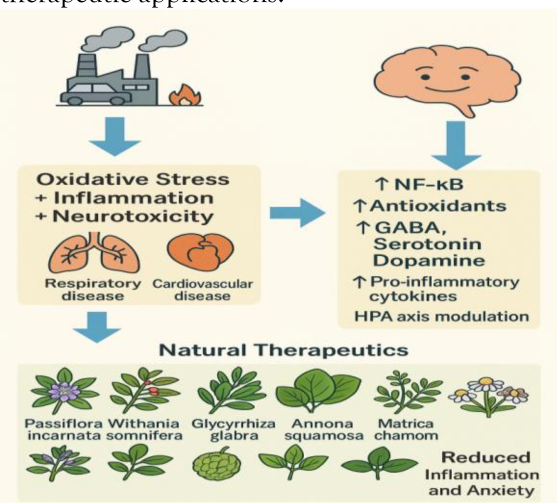
Abstract
Air pollution, particularly fine particulate matter ($PM_{2.5}$), is a major global health concern, contributing to various acute and chronic diseases. $PM_{2.5}$ induces oxidative stress and inflammation, leading to cardiovascular, respiratory, and neuropsychiatric disorders, including anxiety and depression. In India, energy practices significantly contribute to both indoor and outdoor air pollution, highlighting the need for sustainable solutions. Increasing interest in natural therapeutics, particularly medicinal plants, has emerged due to their anti-inflammatory and anxiolytic properties. This review explores the therapeutic potential of nine selected medicinal plants (Passiflora incarnata, Withania somnifera, Glycyrrhiza glabra, Spinacia oleracea, Piper betle, Annona squamosa, Aegle marmelos, Matricaria chamomilla, Ocimum sanctum) and their phytoconstituents in mitigating inflammation and anxiety related to air pollution exposure. Through bibliometric analysis, systematic review, and meta-analysis, we evaluate their mechanisms of action, focusing on molecular pathways like cytokine modulation, NF-κB signaling, antioxidant defense, and neurophysiological regulation. The findings highlight the potential of these plants in addressing both systemic and neurological effects of pollution. However, challenges remain in standardizing dosages and conducting long-term clinical studies. Future research should prioritize dosage standardization, synergistic phytochemical interactions, and extensive clinical trials to optimize their therapeutic use in air pollution-related health issues.
Keywords- *Bibliometric, Study effects, Air pollutants, Oxidative stress, Phenolic compound, Medicinal Plants, phytochemistry, Neuroinflammation, Meta-analysis*

Highlights-Air pollution, particularly $PM_{2.5}$, contributes to inflammation and anxiety via oxidative stress and neuroinflammation. Nine medicinal plants with anti-inflammatory and anxiolytic properties are explored for mitigating pollution-related health impacts. These plants target overlapping pathways involved in immune modulation and neurophysiological regulation. A comprehensive methodology, including bibliometric analysis, systematic review, and meta-analysis, was employed. Findings highlight the potential of botanical medicine as a complementary approach to pollution-related health disorders.
Challenges remain in standardizing dosages, conducting long-term clinical trials, and exploring synergistic phytochemical interactions. Future research should focus on addressing these gaps to optimize therapeutic applications.



Graphical Abstract: *Overview of Air pollution health Impacts and Pathophysiology of Air pollution-induced inflammation and Anxiety*

INTRODUCTION

Air pollution, largely driven by industrialization, urbanization, and unsustainable energy practices, has become one of the foremost global health challenges. It is now well-established that pollutants such as particulate matter ($PM_{2.5}$ and PM_{10}), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), carbon monoxide (CO), ozone (O_3), volatile organic compounds (VOCs), and ammonia (NH_3) play a central role in the pathogenesis of both acute and chronic diseases (Manisalidis et al., 2020; Morakinyo et al., 2017). Fine particulate matter ($PM_{2.5}$), in particular, has the ability to infiltrate the pulmonary alveoli and systemic circulation, initiating oxidative stress and inflammatory responses (Hamanaka et al., 2018; Péter et al., 2015).Multiple studies highlight the health burden linked to prolonged $PM_{2.5}$ exposure, including cardiovascular disease, respiratory illnesses like bronchitis, pneumonia, COPD, and even central nervous system (CNS) disorders such as anxiety and depression (Hedaoo et al., 2021; Costa et al., 2014; Roberts et al., 2019). Research has further revealed that the interplay between $PM_{2.5}$ and environmental factors can enhance the transmission and severity of infectious diseases, such as COVID-19 (Sharma et al., 2024a; Sharma et al., 2022a). These findings are consistent with earlier analyses of air quality trends and pollution-associated health risks in urban India (Upadhyay et al., 2020; Biswas et al., 2011).India's energy practices, especially household cooking methods, contribute significantly to indoor and outdoor air pollution, underscoring the need for systemic changes aligned with Sustainable Development Goals (SDG 7.1.2) (Kumar et al., 2024). The contribution of these pollutants to both physiological and psychological disorders is well documented in recent reviews (Chaitanya et al., 2022). Notably, the inhalation of fine particulates does not only impair lung function but also disrupts neural pathways, leading to neuroinflammation—a proposed mechanism for pollution-induced anxiety and depressive disorders (Costa et al., 2014; Sharma et al., 2022b).

In this context, natural therapeutic strategies are gaining traction. A systematic review emphasized the protective potential of herbal remedies in mitigating lung tissue damage caused by air pollutants (Sharma et al., 2023). Traditional medicinal systems such as Ayurveda, Unani, and Siddha advocate the use of plant-based interventions, many of which exhibit anti-inflammatory and neuroprotective properties (Rizvi et al., 2022; Patwardhan et al., 2014).

Bioactive constituents from plants like *Passiflora incarnata*, *Withania somnifera*, *Glycyrrhiza glabra*, *Spinacia oleracea*, *Piper betle*, *Annona squamosa*, *Aegle marmelos*, *Matricaria chamomilla*, and *Ocimum sanctum* have demonstrated efficacy in modulating inflammation and anxiety-related pathways. These plants hold promise as complementary or alternative therapies in countering the dual burden of pollution-induced physical and mental health challenges.

This review aims to explore the dual role of selected medicinal plants and their phytoconstituents in mitigating both inflammation and anxiety associated with air pollution exposure. Through an integrative lens combining modern science and traditional knowledge, we seek to propose evidence-based, plant-derived solutions to pollution-linked health disorders.

Air Pollution-Induced Inflammation and Anxiety: Mechanisms of Action

Inflammation from Air Pollution

Airborne pollutants such as particulate matter (PM) and nitrogen dioxide (NO_2) initiate a robust inflammatory response upon inhalation. These pollutants activate innate immune cells, most notably alveolar macrophages and neutrophils leading to the release of pro-inflammatory cytokines including tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1 beta (IL-1β) (Sharma et al., 2023). This cytokine cascade promotes systemic inflammation, oxidative stress, and endothelial dysfunction. Prolonged exposure results in chronic pulmonary inflammation, which contributes to the progression of asthma, chronic obstructive pulmonary disease (COPD), and cardiovascular disorders by compromising respiratory barrier function and promoting vascular inflammation.

Air Pollution and Mental Health

Chronic exposure to ambient air pollutants is significantly associated with neuropsychiatric disorders such as anxiety, depression, and cognitive impairment (Péter et al., 2015). The neurotoxic effect is primarily mediated through neuroinflammation—wherein PM crosses the blood-brain barrier (BBB) or activates afferent vagal pathways, stimulating microglial activation. Activated microglia releases inflammatory mediators and reactive oxygen species (ROS), impairing hippocampal neurogenesis and synaptic integrity. Additionally, oxidative stress in neuronal tissues disrupts neurotransmitter balance and exacerbates hypothalamic-pituitary-adrenal (HPA) axis dysregulation, further linking pollution to psychological distress.

Medicinal Plants with Anti-Inflammatory and Anxiolytic Properties

Given the growing recognition of air pollution as a dual threat to respiratory and mental health via systemic inflammation and neurotoxicity, there is a critical need for interventions that can simultaneously counteract both effects. Medicinal plants, with their complex phytochemical profiles, offer promising bioregulatory strategies. Their bioactive constituents such as flavonoids, alkaloids, terpenoids, and phenolic acids interact with key molecular pathways involved in inflammation (NF-κB, COX-2) and neurotransmission (GABAergic, serotonergic systems). Unlike synthetic drugs targeting singular pathways, these phytochemicals exert pleiotropic effects, modulating cytokine release, oxidative stress responses, and neuroendocrine signaling.

In this section, we explore nine medicinal plants known for their anti-inflammatory and anxiolytic properties, which have shown potential in mitigating the health effects of air pollution. These plants have been categorized based on their taxonomical classification, botanical features, geographic distribution, bioactive compounds, and their mechanisms of action related to inflammation and anxiety (see Table 1).

Passionflower (*Passiflora incarnata*): Passionflower is known for its calming effects. It contains flavonoids like apigenin and vitexin, which can modulate gamma-aminobutyric acid (GABA) receptors in the brain, promoting relaxation and reducing anxiety. Additionally, these compounds exhibit anti-inflammatory properties by inhibiting pro-inflammatory cytokines such as TNF-α and IL-6 (Fonseca et al., 2020; Gad et al., 2022).

Ashwagandha (*Withania somnifera*): Ashwagandha is an adaptogenic herb traditionally used in Ayurvedic medicine. Its active components, including withanolides, have been shown to reduce inflammation by downregulating pro-inflammatory pathways like NF-κB. Ashwagandha also modulates GABAergic signaling, contributing to its anxiolytic effects (Afonso et al., 2023; Ignacyk et al., 2023).

Licorice (*Glycyrrhiza glabra*): Licorice root contains glycyrrhizin, a compound with anti-inflammatory properties that suppresses the activity of nuclear factor-kappa B (NF-κB) and reduces the production of pro-inflammatory cytokines. It also has anxiolytic effects through modulation of the hypothalamic-pituitary-adrenal (HPA) axis, helping to regulate cortisol levels (Bisht et al., 2022).

Spinach (*Spinacia oleracea*): Spinach is rich in antioxidants such as flavonoids, carotenoids, and vitamins C and E. These antioxidants help reduce oxidative stress and inflammation by neutralizing free radicals. Spinach's high magnesium content is associated with reduced anxiety levels, supporting its role in mitigating mental health impacts of air pollution (Lasya et al., 2022).

Custard Apple (*Annona squamosa*): Custard apples contain bioactive compounds like acetogenins, alkaloids, and flavonoids, which possess anti-inflammatory and antioxidant properties. These compounds can inhibit the production of inflammatory markers such as IL-6 and TNF-α. Its anxiolytic properties are likely due to modulation of GABAergic transmission (Chen et al., 2017).

Bael (*Aegle marmelos*): Bael is traditionally used to treat respiratory and inflammatory conditions. It contains coumarins and flavonoids that exhibit anti-inflammatory effects by modulating pathways like NF-κB. Bael also has calming effects, possibly through interaction with serotonin and dopamine pathways, contributing to its anxiolytic potential (Jagetia et al., 2023).

Chamomile (*Matricaria chamomilla*): Chamomile is widely recognized for its calming and anti-anxiety effects, largely due to its high content of apigenin, a flavonoid that binds to GABA receptors. It also exhibits anti-inflammatory properties by reducing the production of pro-inflammatory cytokines and inhibiting the NF-κB pathway (Srivastava et al., 2010).

Betel (*Piper betle*): Betel leaves are rich in polyphenols, which have antioxidant and anti-inflammatory properties. These compounds help reduce oxidative stress and inhibit the production of pro-inflammatory cytokines. Betel also has anxiolytic effects, potentially through interaction with neurotransmitter systems like GABA and serotonin (Biswas et al., 2022, Alam et al., 2013).

Holy Basil (*Ocimum sanctum*): Holy basil, or tulsi, is revered in Ayurveda for its adaptogenic and anti-inflammatory properties. It contains eugenol, ursolic acid, and rosmarinic acid, which help combat inflammation by inhibiting pro-inflammatory pathways. Tulsi also helps reduce anxiety through its effects on the HPA axis and neurotransmitter systems, and its antioxidant properties protect against oxidative stress caused by air pollutants (Srivastava et al., 2021).

Table 1: Medicinal Plants including Anti-Inflammatory, Anxiolytic Properties and Health Applications

Common Name (Scientific Name)	Taxonomical Classification	Botanical Features	Geographic Distribution	Bioactive Compounds	Mechanism of Action		Health Applications	References
					Anti-inflammatory	Anxiolytic		
Passionflower (*Passiflora incarnata*)	Plantae; Magnoliophyta; Magnoliopsida; Malpighiales; Passifloraceae	Perennial vine with purple-blue flowers and lobed leaves	Southeastern USA, South America	Flavonoids (apigenin, vitexin), alkaloids, GABA-like compounds	Downregulates TNF-α and IL-6	Binds to GABA-A receptors	Reduces inflammation and anxiety due to pollution	Kaikade et al., 2023; Fonseca et al., 2020; Gad et al., 2022
Ashwagandha (*Withania somnifera*)	Plantae; Magnoliophyta; Magnoliopsida; Solanales; Solanaceae	Woody shrub with green-yellow flowers and red berries	India, North Africa, Middle East	Withanolides, sitoindosides, alkaloids	Inhibits NF-κB and cytokines	Modulates GABAergic and serotonergic systems	Counters stress-induced inflammation	Mikulska et al., 2023; Afonso et al., 2023; Ignacyk et al., 2023; Devarasetti et al., 2024
Licorice (*Glycyrrhiza glabra*)	Plantae; Magnoliophyta; Magnoliopsida; Fabales; Fabaceae	Herb with compound leaves and purple-blue flowers	Europe, Asia	Glycyrrhizin, glabridin, flavonoids	Suppresses NF-κB, COX-2, cytokines	Supports adrenal function, GABA modulation	Eases airway inflammation and anxiety	Sharifi-Rad et al., 2021; X. Ji et al., 2024; Hasan et al., 2021; Pastorino et al., 2018
Spinach (*Spinacia oleracea*)	Plantae; Magnoliophyta; Magnoliopsida; Caryophyllales; Amaranthaceae	Leafy vegetable with broad green leaves	Temperate regions globally	Flavonoids, carotenoids, vitamin C, magnesium	Neutralizes ROS, inhibits COX/LOX	Supports neurotransmitter balance via magnesium	Protects lungs, improves mood regulation	Lasya et al., 2022; Wang et al., 2024; Ramalingum et al., 2014
Custard Apple (*Annona squamosa*)	Plantae; Magnoliophyta; Magnoliopsida; Magnoliales; Annonaceae	Tree with green scaly fruits and sweet pulp	Tropical Americas, Asia, Africa	Acetogenins, flavonoids, alkaloids	Downregulates IL-6, TNF-α	Modulates GABAergic signaling	Combats neuroinflammation and calms CNS	Chen et al., 2017; Sandeep et al., 2017; Mittal et al., 2017
Bael (*Aegle marmelos*)	Plantae; Magnoliophyta; Magnoliopsida; Sapindales; Rutaceae	Deciduous tree with fragrant leaves and hard fruits	India, Southeast Asia	Coumarins, flavonoids, tannins	Inhibits COX-2 and TNF-α	Stimulates GABAergic and serotonergic activity	Reduces airway inflammation and stress	Jagetia et al., 2023; Pathirana et al., 2020
Chamomile (*Matricaria chamomilla*)	Plantae; Magnoliophyta; Magnoliopsida; Asterales; Asteraceae	Herbaceous plant with daisy-like flowers	Europe, Western Asia	Apigenin, bisabolol, chamazulene	Reduces COX-2, TNF-α via NF-κB inhibition	Apigenin binds to GABA-A receptors	Herbal tea for inflammation, calming agent	Srivastava et al., 2010; Sah et al., 2022
Betel (*Piper betle*)	Plantae; Magnoliophyta; Magnoliopsida; Piperales; Piperaceae	Vine with heart-shaped glossy leaves	India, Southeast Asia	Eugenol, chavicol, alkaloids, polyphenols	Inhibits IL-6 and TNF-α	Acts as GABA receptor modulator	Traditional remedy for inflammation and anxiety	Singh et al., 2017; Gulhane et al., 2015
Holy Basil (*Ocimum sanctum*)	Plantae; Magnoliophyta; Magnoliopsida; Lamiales; Lamiaceae	Aromatic herb with green/purple leaves	India, Asia, Africa	Eugenol, ursolic acid, rosmarinic acid, luteolin	Inhibits COX-2, TNF-α, IL-6, CRP	Modulates HPA axis, GABA, serotonin	Mitigates oxidative lung damage and stress	Jamshidi et al., 2017; Srivastava et al., 2021

Mechanisms of Action and Pathways of Medicinal Plants in the Reduction of Inflammation and Anxiety

The therapeutic potential of medicinal plants in combating inflammation and anxiety primarily stems from their ability to target overlapping molecular and cellular pathways involved in immune modulation and neurophysiological regulation. In inflammatory conditions, these plants act through mechanisms such as the inhibition of pro-inflammatory cytokines (such as TNF-α, IL-6, IL-1β), suppression of transcription factors like NF-κB, and enhancement of antioxidant defense systems including superoxide dismutase (SOD) and glutathione peroxidase (GPx). These effects are crucial in counteracting inflammation induced by environmental pollutants and oxidative stress (Biswas et al., 2022; Rezaei et al., 2024).

In terms of anxiolytic effects, the bioactive compounds found in these medicinal plants modulate central nervous system (CNS) activity through various pathways. They enhance GABAergic neurotransmission, elevate serotonin and dopamine levels, reduce cortisol (a stress hormone), and suppress neuroinflammation by inhibiting microglial activation. Some also promote neurogenesis and synaptic plasticity, providing resilience against stress-related neurodegeneration (Srivastava et al., 2010; Wang et al., 2023).

Figure 1 illustrates the complex interactions for core anti-inflammatory and anxiolytic pathways modulated by the nine selected medicinal plants. These pathways converge at key molecular nodes including cytokine signaling, oxidative stress response, neurotransmitter modulation, and HPA axis regulation. Supplementary Table 1 further summarizes the mechanisms of action for each of the nine selected plants, linking specific bioactive compounds to their respective anti-inflammatory and anxiolytic biomarkers.

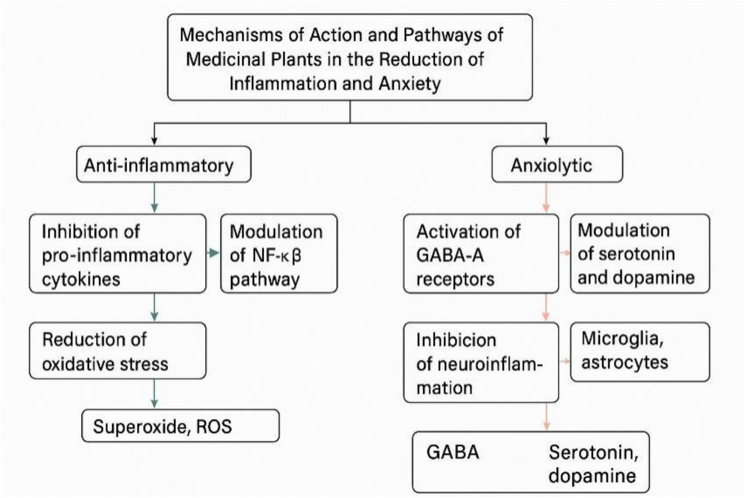


Figure 1. *Mechanisms of action and pathways of medicinal plants in the reduction of inflammation and anxiety.*

METHODOLOGY

Data Harvesting and Materials: This review employs a bibliometric and systematic literature analysis to evaluate research trends on the dual role of medicinal plants in reducing inflammation and anxiety caused by air pollution.

Data Sources and Search Strategy: Data were sourced from prominent scientific databases, including Scopus, Web of Science, PubMed, Cochrane Library, and Google Scholar. The literature search was conducted using search terms such as "medicinal plants," "air pollution," "anti-inflammatory," and "anxiolytic" from the last 10 years (2014 to 2024) were exported from Scopus in RIS format and imported into Mendeley for reference management. Duplicate entries were removed, and the articles were categorized by plant species and effects. In addition, for a comprehensive review, keywords like "air pollution-induced inflammation," "medicinal plants and inflammation," "herbal remedies for anxiety," and "meta-analysis on herbal medicine and pollution-related diseases" were used. The search aimed to retrieve peer-reviewed articles, clinical trials, in vivo and in vitro studies investigating the effects of medicinal plants on inflammation and anxiety induced by air pollution.

Inclusion and Exclusion Criteria: The inclusion criteria focused on peer-reviewed studies, clinical trials, and experimental studies that investigated the effects of medicinal plants on inflammation and anxiety, specifically in the context of air pollution. Studies that did not examine air pollution-related health effects, review articles (unless providing background information), and non-English articles (without available translations) were excluded.

Data Extraction: The data extraction process involved collecting information on study type, sample size, medicinal plant species used, biomarkers of inflammation (e.g., C-reactive protein, interleukin-6, tumor necrosis factor-alpha, and oxidative stress markers), and anxiety assessment tools (e.g., Generalized Anxiety Disorder-7, Hamilton Anxiety Rating Scale, and cortisol levels).

Quality Assessment: Quality assessment of included studies was carried out using PRISMA guidelines. The risk of bias for individual studies was evaluated using the Cochrane Risk of Bias Tool.

Medicinal Plants for Review: The review focuses on nine medicinal plants previously detailed in Section 3, selected for their reported anti-inflammatory and anxiolytic effects relevant to air pollution-induced health conditions. These include *Passiflora incarnata*, *Withania somnifera*, *Glycyrrhiza glabra*, *Spinacia oleracea*, *Piper betle*, *Annona squamosa*, *Aegle marmelos*, *Matricaria chamomilla*, and *Ocimum sanctum*. Specific plant parts such as flowers, roots, and leaves were analyzed based on their therapeutic potential and relevance to the study's objectives (Table 1 & Supplementary Table 1).

Systematic Review Process: The PRISMA flow diagram was designed to illustrate the selection process, adapted from the PRISMA 2020 guidelines (Page et al., 2021). A total of 500 records were identified through database searches. After removing 80 duplicates, 420 records were screened. Following the exclusion of 288 articles based on title and abstract, 132 full-text reports were sought, of which 50 could not be retrieved. Of the remaining 82 assessed for eligibility, 52 were excluded for not meeting inclusion criteria. Ultimately, 30 studies were included in the final review and meta-analysis.

Bibliometric Analysis: Bibliometric indicators such as publication count, citation analysis, and keyword frequency were extracted to evaluate trends in the research. VOSviewer (Larcon-Ruiz et al., 2023) and CiteSpace tools were employed to visualize co-authorship networks, keyword clusters, and emerging research trends. Data were cross-checked across multiple databases to ensure reliability and reproducibility.

Meta-Analysis: A meta-analysis was conducted to estimate the effect sizes of medicinal plants on inflammation and anxiety related to air pollution. Various statistical methods were employed to calculate effect sizes and visualize the results.

Synthesis of Findings: The results of the meta-analysis will provide insight into the potential of medicinal plants as natural interventions for reducing the harmful health effects of air pollution. The discussion will explore the relationship between air pollution, oxidative stress, and inflammation, as well as the efficacy of medicinal plants in addressing these issues.

The review will also highlight the limitations of current research and propose future research directions, emphasizing the need for well-designed clinical trials.

Research Methodology Standards: This review follows the systematic review methodology outlined by Haddaway et al. (2022) and Donelli et al. (2019) to ensure rigorous and transparent research standards. All references are formatted according to APA referencing guidelines.

Systematic Review Process

Prisma Systematic Review

In total, 500 research articles were identified initially through the comprehensive keyword-based search strategy from the last 10 years (2014 to 2024). After removing 80 duplicates using reference management tools, 420 unique articles remained for screening. Title and abstract screening led to the exclusion of 288 articles due to reasons such as lack of focus on both inflammation and anxiety, irrelevance to air pollution-induced health conditions, or poor methodological frameworks. Full-text access was sought for 132 records, but 50 could not be retrieved due to paywall restrictions, broken links, or language barriers.

Following a full-text review of 82 studies, 52 were excluded for reasons including lack of relevance to the selected medicinal plants or failure to address both inflammation and anxiety. Ultimately, 30 studies were included in the final review, as they specifically examined the dual therapeutic effects of the selected medicinal plants in the context of air pollution-induced inflammation and anxiety, supported by biochemical or physiological biomarker data. Figure 2 shows PRISMA flow diagram illustrating the study selection process, adapted from the PRISMA 2020 guidelines (Page et al., 2021).

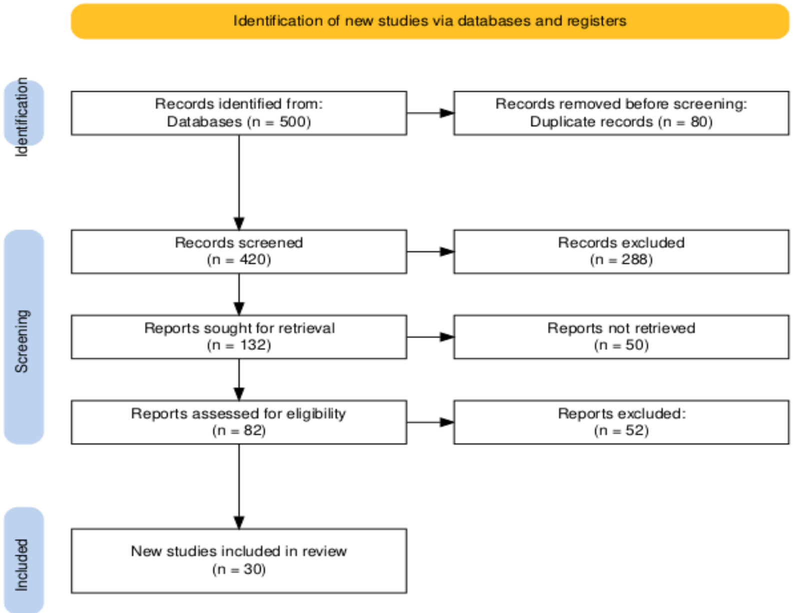


Figure 2. PRISMA Flow-Diagram

Bibliometric and Systematic Analysis

A bibliometric analysis was performed using VOSviewer to identify research trends, thematic concentrations, and knowledge gaps in the intersection of medicinal plants, inflammation, anxiety, and air pollution. The analysis revealed significant clustering of research activity, demonstrating the interdisciplinary nature of this field. Specifically, the keyword co-occurrence map (Figure 3a) included 305 items, 22,035 links, a total link strength of 96,917, and 4 distinct thematic clusters. These clusters are visually differentiated by color and represent clinical efficacy of plant-based treatments (blue), traditional and ethnobotanical knowledge (red), phytochemical and antioxidant activity (green), and the health impacts of air pollution (yellow). This visualization underscores the growing integration of biomedical, pharmacological, environmental, and ethnobotanical domains in addressing air pollution-induced health issues. The review synthesized both the bibliometric findings and evidence from selected studies to offer a comprehensive overview of the dual roles of medicinal plants in mitigating inflammation and anxiety related to air pollution. A structured systematic study plan from 2014 to 2024 was employed. Between 2014 and 2016, focus was placed on identifying key pollutants and their physiological impacts. From 2016 to 2018, research shifted toward the documentation and evaluation of medicinal plants and their active compounds. Between 2018 and 2020, clinical and preclinical studies on herbal interventions were collected and assessed. From 2020 to 2022, meta-analyses and statistical modeling (including regression analyses) were conducted to evaluate intervention effectiveness. The final phase, spanning 2022 to 2024, involved synthesizing results, identifying future research directions, and generating recommendations for leveraging plant-based therapies to counteract pollution-related inflammatory and anxiety disorders.

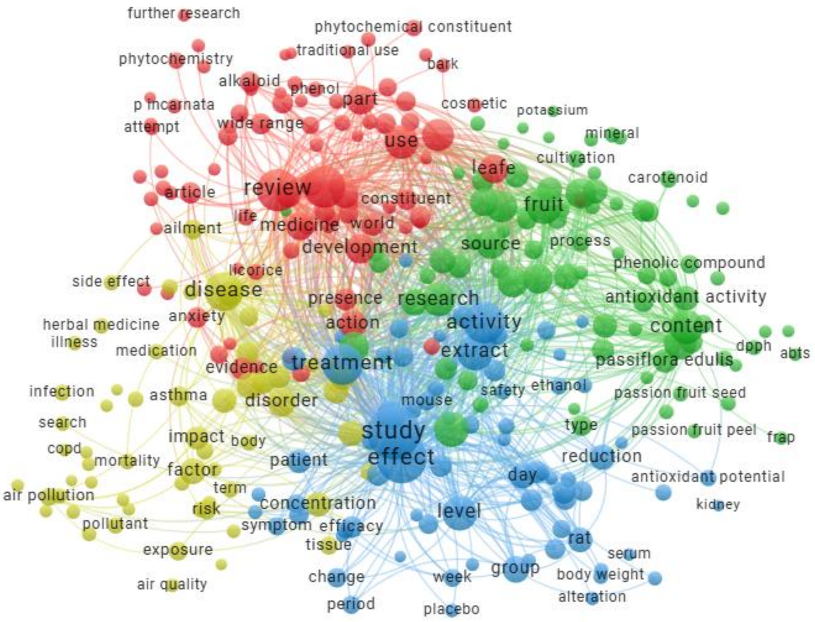


Figure 3. Network visualization

Therapeutic Evaluation of Medicinal Plants Using Radar Chart

Nine selected medicinal plants were evaluated using five therapeutic criteria: anti-inflammatory activity, anxiolytic action, antioxidant capacity, clinical evidence support, and phytochemical richness. Each criterion was defined and scored on a 1–5 scale based on a comprehensive literature review of in vitro, in vivo, and clinical studies. Quantitative metrics (e.g., IC_{50} values, measured neurotransmitter levels) were used when available; otherwise, scores were assigned qualitatively. Data were collected from systematic searches of PubMed, Scopus, and Google Scholar, emphasizing recent publications and meta-analyses. The resulting scores for each plant by criterion are given below:

Anti-inflammatory Activity: This criterion assesses the ability of a plant to suppress pro-inflammatory mediators. Key endpoints include reductions in TNF-α, IL-6, IL-1β, or COX-2 as measured in biochemical

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or cellular assays (Aggarwal & Harikumar, 2009; Tripathi et al., 2021). Plants with strong evidence of inhibiting these targets received higher scores (e.g., significant COX-2 inhibition in vitro yields a top score).

Anxiolytic Action: Based on modulation of central nervous system neurotransmitters. Enhancing GABAergic signaling or serotonergic activity is indicative of anxiolytic potential (Bhattacharya et al., 2000; Grundmann et al., 2008). For example, *Passiflora incarnata* exerts anxiolytic effects via the GABAergic system (Akhondzadeh et al., 2001).

Antioxidant Capacity: Evaluated using standard assays like DPPH, FRAP, ABTS, and ROS scavenging activity (Apak et al., 2016). A lower IC_{50} or higher Trolox-equivalent value indicates greater antioxidant capacity.

Clinical Evidence Support: Reflects the quality and number of human clinical trials. Randomized controlled trials with defined dosages and measurable outcomes were prioritized (Panossian & Wikman, 2010; Lopresti et al., 2019). For example, clinical trials have shown *Withania somnifera* significantly reduces markers of inflammation and stress in patients.

Phytochemical Richness: Refers to the number and diversity of bioactive compounds such as alkaloids, flavonoids, terpenes, and phenolic acids (Tungmunnithum et al., 2018). Plants with a broader spectrum of these compounds received higher scores.

Table 2 summarizes the scoring results across these five parameters. To visualize the comparative profiles, a radar plot (Figure 4) maps the five scores for each plant on a pentagonal grid. For instance, *Withania somnifera* (orange trace) demonstrates a large profile, indicating strong anti-inflammatory and antioxidant activities, supported by evidence of TNF-α, IL-6, and COX-2 suppression (Choudhary et al., 2017). In contrast, *Matricaria chamomilla* has a distinct peak on the anxiolytic axis, aligning with its known GABA-modulating effects (Amsterdam et al., 2009). The layout of the radar plot allows for immediate identification of dual-action or multi-functional herbs. Radar chart visualization, as seen in multivariate profiling studies, enhances pattern recognition and comparative analysis (Chen et al., 2021). Data were gathered through comprehensive literature mining, using combinations of each plant's name with keywords like "anti-inflammatory," "anxiety," "clinical trial," and "phytochemicals." The final scoring synthesizes high-quality evidence to highlight herbs with strong potential in managing inflammation and anxiety simultaneously.

Table 2. *Evaluation Table for Radar Chart (Score: 1–5) (Scale: 1 = low, 5 = high; based on literature reviews)*

Plant Name	Anti-inflammatory	Anxiolytic	Antioxidant	Clinical Support	Phytochemical Richness
Withania somnifera	5	5	4	5	4
Passiflora incarnata	2	5	3	4	3
Glycyrrhiza glabra	5	3	5	4	4
Spinacia oleracea	3	2	5	3	3
Piper betle	4	3	4	2	4
Annona squamosa	3	4	3	3	3
Aegle marmelos	4	3	4	3	3
Matricaria chamomilla	3	4	4	4	3
Ocimum sanctum	5	4	5	5	5

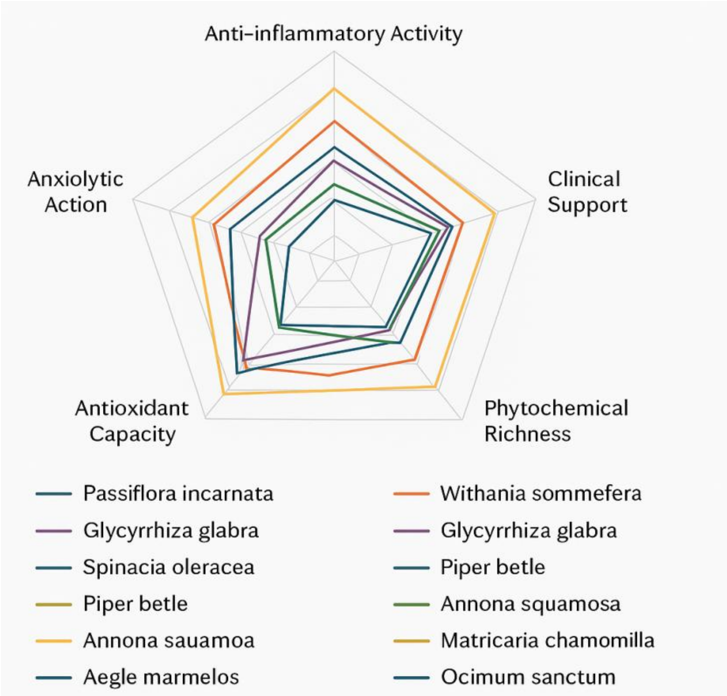

Figure 4. *Radar chart comparing therapeutic scores for nine medicinal plants across five criteria. Each plant's polygon connects scores for Anti-inflammatory Activity, Anxiolytic Action, Antioxidant Capacity, Clinical Support, and Phytochemical Richness. Differences in area and shape illustrate relative strength across dimensions.*

Statistical Analysis

Statistical analysis was performed to summarize and interpret the bibliometric and experimental data. Descriptive statistics were used to analyze publication trends, citation counts, and keyword occurrences. For bibliometric network analysis, metrics such as degree centrality and clustering coefficients were calculated using a VOS viewer.

Correlation analysis

The scatter plot in Figure 5 demonstrates a clear positive correlation between ambient $PM_{2.5}$ concentrations (ranging from 20 μg/m³ to 200 μg/m³) and biological markers associated with inflammation and anxiety. Red markers represent inflammatory biomarkers—such as C-reactive protein (CRP) and interleukin-6 (IL-6)—while blue markers indicate anxiety-related scores, potentially reflecting cortisol levels or behavioral assessments. As $PM_{2.5}$ levels increase, both inflammation markers and anxiety scores rise in a roughly linear trend, indicating that higher pollution exposure is associated with greater biological stress responses.

This dual upward trend supports existing literature suggesting that air pollution acts as a systemic stressor impacting both physiological and psychological health. Fonken et al. (2011) observed increased anxiety-like behaviors and hippocampal cytokine expression in rodent models chronically exposed to air pollution, pointing to a neuroinflammatory mechanism. Similarly, Thomson (2019) highlighted how elevated allostatic load from environmental pollutants contributes to mental health deterioration, including heightened risks of anxiety and depression.

These findings underscore the necessity of addressing pollution as a multifaceted public health concern. Moreover, the simultaneous rise in inflammation and anxiety markers justifies further investigation into phytotherapeutic strategies. Medicinal plants like *Withania somnifera* (Ashwagandha), *Ocimum sanctum* (Tulsi), and *Curcuma longa* (Turmeric) possess both anti-inflammatory and anxiolytic effects. Bhattacharya et al. (2000) demonstrated the neuroprotective benefits of Ashwagandha in animal models, while Tiwari and Dwivedi (2017) compiled evidence for the anti-inflammatory efficacy of several botanical species.

Overall, this figure visually reinforces the intertwined nature of environmental and biological stress and highlights the potential of botanical medicine as a complementary approach to mitigating pollution-related health impacts.

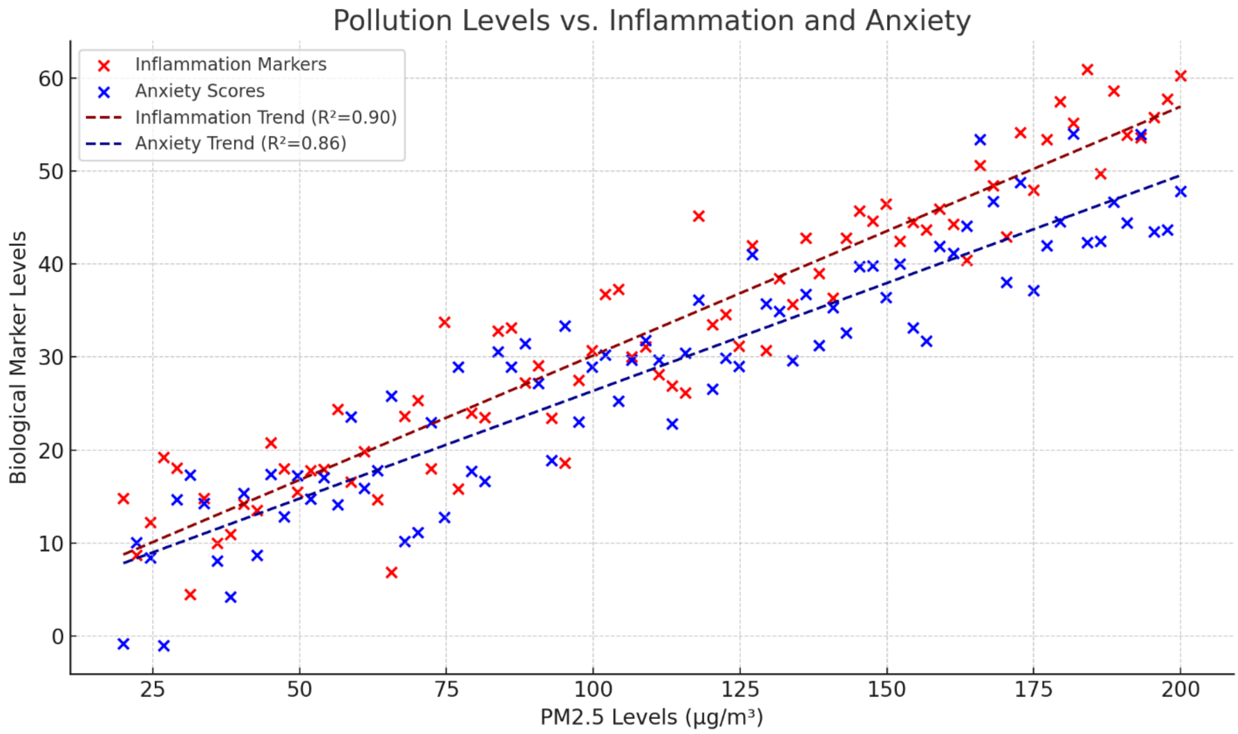

Figure 5: *Scatter plot with regression trend lines illustrates a clear positive correlation between ambient $PM_{2.5}$ concentrations and biological markers of inflammation and anxiety.*

Regression analysis

The scatter plot (Figure 4) shows the relationship between ambient $PM_{2.5}$ concentrations (x-axis) and biological marker levels associated with inflammation (red crosses) and anxiety (blue crosses). Both outcome variables exhibit strong positive linear correlations with pollution levels. Linear regression yielded coefficients of determination (R^2) of 0.90 for inflammation markers and 0.86 for anxiety scores, indicating that higher $PM_{2.5}$ exposure is strongly associated with elevated inflammatory and anxiety-related biomarkers. These findings are consistent with previous research demonstrating that air pollution induces systemic inflammation and psychological stress through neuroimmune mechanisms (Fonken et al., 2011; Thomson, 2019). The concurrent increase in both inflammation and anxiety markers supports the hypothesis that air pollution acts via overlapping pathophysiological pathways, reinforcing the case for dual-targeted phytotherapeutic interventions using medicinal plants with both anti-inflammatory and anxiolytic properties.

Limitations

While evidence supports the therapeutic potential of medicinal plants, several limitations hinder comprehensive understanding of their dual role in mitigating inflammation and anxiety, particularly under air pollution exposure. Few studies simultaneously evaluate anti-inflammatory and anxiolytic effects within pollution-relevant models, and mechanistic integration, especially involving oxidative stress and neurotransmitter regulation, is limited. Standardized protocols for plant extract characterization and dosing are lacking, affecting reproducibility. Research on synergistic plant combinations, bioavailability, pharmacokinetics, and advanced delivery systems (e.g., nanoparticles) remains scarce. Most findings are preclinical, with minimal clinical validation in polluted settings. Additionally, the gut-brain axis, a critical link in pollution-induced neuroinflammation, is underexplored. There is also limited use of advanced analytical tools (e.g., HPLC, FTIR, mass spectrometry) and specific biomarkers to assess pollution-related damage. Integrated, translational research is needed to address these gaps and optimize the therapeutic application of medicinal plants in pollution-linked health disorders.

Ethics Statement

This bibliometric review utilized only publicly available data from established databases such as Scopus and Web of Science. No human or animal subjects were involved, and ethical approval was not required. All sources are properly cited, and the methodology is transparently described to ensure academic integrity and reproducibility.

Challenges and Future Directions

While medicinal plants show promise in alleviating air pollution-induced inflammation and anxiety, key challenges remain. Standardization of dosages, extraction methods, and active constituents is essential to ensure reproducibility and efficacy. Additionally, long-term clinical trials in high-risk, pollution-exposed populations are lacking and urgently needed. Future research should explore synergistic interactions between phytochemicals, aiming to enhance combined anti-inflammatory and anxiolytic effects. Advances in personalized medicine also present opportunities to tailor plant-based interventions based on individual genetic and environmental factors, optimizing therapeutic outcomes.

CONCLUSION

This review demonstrates that medicinal plants possess significant potential as complementary agents in mitigating the dual impact of air pollution on inflammation and anxiety. The nine selected plants exhibit a convergence of anti-inflammatory, antioxidant, and anxiolytic properties through well-documented molecular mechanisms, including cytokine modulation, neurochemical regulation, and oxidative stress reduction. Given the escalating global health burden of $PM_{2.5}$-related diseases, integrating phytotherapeutic strategies offers a promising avenue alongside conventional interventions. Nonetheless, further research is essential to standardize formulations, validate long-term safety and efficacy, and investigate synergistic interactions among phytochemicals. Bridging these gaps will be critical for translating traditional botanical knowledge into evidence-based, scalable health solutions.

CONFLICT OF INTEREST

The authors declare no conflicts of interest in relation to this work. All findings and interpretations are based solely on the data collected and analyzed independently by the authors. This research was not influenced by any external organizations or entities.

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Supplementary Table 1. *Mechanisms of Action of Nine Selected Medicinal Plants in Inflammation and Anxiety Reduction with Biomarkers*

S. No.	Common Name (Scientific Name)	Part Used	Key Compounds	Associated Diseases	Anti-inflammatory Mechanism	Anxiolytic Mechanism	Anti-inflammatory Biomarkers	Anxiolytic Biomarkers	References
1	Passion flower (*Passiflora incarnata*)	Flowers	Flavonoids (vitexin, chrysin), harmala alkaloids	Asthma, bronchitis, COPD, anxiety disorders	Inhibits cytokines, reduces oxidative stress	Acts on GABA receptors	↓ TNF-α, ↓ IL-6, ↓ NF-κB, ↓ COX-2	↑ GABA, ↓ cortisol	Janda et al., 2020; Gad et al., 2022; Fonseca et al., 2020
2	Ashwagandha (*Withania somnifera*)	Roots	Withanolides (withaferin A), alkaloids	Asthma, CVD, depression, anxiety	Suppresses NF-κB, antioxidant, immunomodulatory	Enhances GABAergic activity, lowers cortisol	↓ IL-1β, ↓ IL-6, ↓ TNF-α, ↓ COX-2	↑ GABA, ↑ BDNF, ↓ cortisol	Rezaei et al., 2024; Khurana et al., 2024; Mikulska et al., 2023
3	Licorice (*Glycyrrhiza glabra*)	Roots	Glycyrrhizin, liquiritigenin	Asthma, stress-related anxiety, amnesia	Inhibits COX-2, reduces cytokines	Modulates GABA, dopamine pathways	↓ IL-1β, ↓ TNF-α, ↓ COX-2	↑ GABA, ↑ dopamine, ↓ cortisol	Wang et al., 2023; Meng et al., 2019; Bisht et al., 2021
4	Spinach (*Spinacia oleracea*)	Leaves	Quercetin, kaempferol, carotenoids	COPD, lung cancer, chronic stress	Reduces cytokines, boosts antioxidants	Enhances brain antioxidant status	↓ TNF-α, ↓ IL-6, ↑ SOD, ↑ glutathione	↑ GABA, ↑ BDNF, ↓ cortisol	Kazimierova et al., 2021; Shin et al., 2019
5	Betel Leaf	Leaves	Eugenol, hydroxychavicol,	Respiratory	Inhibits pro-inflammat	GABAergic	↓ TNF-α, ↓ IL-	↑ GABA, ↓	Bhardwaj et al., 2022;

	(*Piper betle*)		β-caryophyllene	infections, anxiety	ory enzymes	modulation	6, ↓ COX-2	cortisol	Rintu et al., 2015
6	Custard Apple (*Annona squamosa*)	Leaves	Flavonoids, acetogenins, ascorbic acid	COPD, asthma, depression, anxiety	Antioxidant and anti-inflammatory	Calming CNS effect	↓ TNF-α, ↓ IL-6, ↑ catalase, ↑ SOD	↑ GABA, ↓ cortisol	Awada et al., 2023; Chavan et al., 2024
7	Bael (*Aegle marmelos*)	Leaves	Flavonoids, skimmianine, linalool	Bronchitis, asthma, anxiety	Inhibits inflammatory mediators	Modulates neurotransmitters	↓ TNF-α, ↓ COX-2, ↑ antioxidants	↑ GABA, ↓ cortisol	Jain et al., 2023; Rajeshkannan et al., 2014
8	Chamomile (*Matricaria chamomilla*)	Flowers	Apigenin, bisabolol, sesquiterpenes	Asthma, bronchitis, sleep disorders	Anti-inflammatory and antioxidant	Binds GABA receptors	↓ IL-6, ↓ TNF-α, ↑ SOD	↑ GABA, ↑ serotonin	Srivastava et al., 2010; Sah et al., 2022
9	Holy Basil (*Ocimum sanctum*)	Leaves	Eugenol, ursolic acid, linalool	Asthma, CVD, neuroinflammation	Downregulates cytokines	Boosts GABA and serotonin	↓ IL-6, ↓ COX-2, ↑ SOD	↑ GABA, ↑ serotonin	Mirje et al., 2014; Jamshidi et al., 2017

Supplementary Table 2. *Scoring Parameters (1–5 Scale)*

Criteria	Description
1. Anti-inflammatory Activity	Based on the plant's ability to suppress inflammatory mediators (e.g., TNF-α, IL-6, COX-2)
2. Anxiolytic Action	The presence of bioactive compounds that modulate neurotransmitters like GABA, serotonin, etc.
3. Antioxidant Strength	Assessed via reported DPPH, FRAP, and ABTS assays or ROS scavenging in cell/tissue models
4. Clinical Evidence Support	Strength of published clinical trials, dosage standardization, and human outcome reports
5. Phytochemical Richness	Number and potency of active compounds (alkaloids, flavonoids, terpenes, etc.) identified