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Exploring the Medicinal Potential of Ageratum conyzoides L.: A Systematic Review

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ABSTRACT

Background

Herbal medicine represents one of the oldest therapeutic systems, utilizing plant-derived active ingredients with origins in ancient Chinese, Greek, Egyptian, and Indian medical traditions. Ageratum conyzoides L. (Asteraceae), commonly known as "billygoat weed," "goat weed," or "bandotan" in Indonesia, is widely distributed across subtropical and tropical regions. The genus name derives from Greek terms "a geras" (meaning "stay young") and "konyzoides" (meaning "plants"), reflecting its historical use in anti-aging applications. Native to tropical America, this invasive herbaceous species has been traditionally employed across Africa for treating fever, constipation, wound care, and ulcers. In West African nations including Togo and Nigeria, A. conyzoides has been utilized for diverse therapeutic purposes ranging from snakebite treatment and measles management to dermatologicalconditions, gastrointestinal disorders, and even purported HIV/AIDS treatment.

Objective

This systematic review aims to synthesize current knowledge on the phytochemical composition, pharmacological properties, extraction methodologies, and clinical applications of Ageratum conyzoides, while evaluating its safety profile and potential therapeutic applications in modern pharmaceutical development.

Methods

A comprehensive literature review was conducted examining peer-reviewed publications, botanical databases, and pharmacological studies on A.conyzoides. Focus areas included phytochemical composition, extraction techniques, in vitro and in vivo pharmacological studies, toxicological assessments, and clinical applications.

Key Findings

Phytochemical analysis of A. conyzoidesextractsrevealedSubstantial concentrations of bioactive compounds including flavonoids (0.97-0.98%), saponins (0.97-0.98%), alkaloids (0.90%), with lower levels of tannins (0.187-0.188%) and phenols (0.022%). Advanced analytical techniques identified diverse secondary metabolites including kaempferol, quercetin, echinatine, precocene derivatives, and various terpenoids. Pharmacological studies demonstrated significant antimicrobial, antioxidant, anti-inflammatory, and antifungal activities, supporting traditional medicinal applications. However, toxicological studies identified concerns regarding hepatotoxic pyrrolizidine alkaloids, particularly in essential oil preparations.

Conclusion

Ageratum conyzoides represents a promising medicinal plant with substantial pharmacological potential substantiated by both traditional use and contemporary scientific investigation. The diverse phytochemical profile supports multiple therapeutic applications, particularly in antimicrobial, antioxidant, and anti-inflammatory therapies. However, careful evaluation of safety protocols, standardization of extraction methods, and further clinical investigations are essential before broader pharmaceutical development and clinical translation.

Keywords: Ageratum conyzoides, phytochemical analysis, pharmacological properties, medicinal plants, systematic review, Asteraceae

I. INTRODUCTION

1.1 Botanical Description and Classification

Ageratum conyzoides L. is a pervasive annual herbaceous plant originating from tropical America, particularly Brazil[1]. This invasive species typically grows to heights of approximately one meter and is characterized by ovate leaves measuring 2-6 cm in length, bearing flowers ranging in color from white to mauve. The plant can be distinguished from its closely related species Ageratum houstonianum by finer hair distribution on stems and unique flower morphology[1][2].

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Taxonomic Classification:

Fig No 1: A. conyzoides

Category	Classification
Kingdom	Plantae
Phylum	Tracheophyta
Class	Magnoliopsida
Order	Asterales
Family	Asteraceae
Genus	Ageratum
Species	Ageratum conyzoides L.

1.2 Physical Characteristics

- **Height:** Up to 1 meter (3.3 feet)
- **Stems and Leaves:** Covered with fine white hairs
- **Leaf Morphology:** Ovate with broad base; length up to 7.5 cm
- **Inflorescence:** Purple, blue, pinkish, or white flowers; <6 mm diameter; arranged in terminal flower-heads
- **Fruits:** Small brown one-seeded achenes dispersed via seed

1.3 Distribution, Habitat, and Ecological Impact

Native Range: Central and South America, West Indies
Naturalized Distribution: Throughout Asia, temperate Brazil, and most African regions (excluding arid areas) [1][3]
Habitat Preferences: Moist uplands, hydromorphic lands, shade-flooded areas, and disturbed agricultural sites [1][3][4]

A. conyzoides has established itself as a significant ecological threat in various regions. In Asia, particularly in rice-growing regions, this species is classified as a moderate agricultural weed, aggressively competing with native flora and reducing biodiversity. Studies conducted in the Shivalik hills of Himachal Pradesh, India, documented that A. conyzoides invasion resulted in a 32.10% reduction in average plant species numbers, a 41.21% decline in overall species diversity, and substantial decreases in dry biomass of affected ecosystems[1]. These ecological impacts underscore the necessity for effective management strategies combining physical removal, chemical control, flame weeding, mulching, and biological control approaches [1][5].

1.4 Traditional Medicinal Applications

Across diverse geographical regions and cultures, A. conyzoides has occupied a significant place in traditional medicine systems. The plant's therapeutic applications span multiple organ systems and pathological conditions:

- Wound healing and burn treatment through direct poultice application
- Fever reduction and antipyretic effects
- Rheumatism and arthritis management via anti-inflammatory properties
- Gastrointestinal disorders including dysentery, diarrhea, colic, and ulcers
- Respiratory conditions such as pneumonia and asthma
- Gynecological applications for menstrual irregularities and vaginal infections

- Dermatological conditions including eczema and ringworm
- Oral hygiene maintenance through traditional mouthwash preparations

However, despite these therapeutic applications, A. conyzoides contains toxic pyrrolizidine alkaloids including lycopsamine and echinatine, which are associated with severe hepatotoxicity and potential carcinogenic effects [2][6]. This dual nature—therapeutic potential coupled with toxicological risks—necessitates careful research and standardized usage guidelines.

II. PHYTOCHEMICAL COMPOSITION AND SECONDARY METABOLITES

2.1 Overview of Bioactive Compounds

Ageratum conyzoides contains a diverse array of phytochemicals contributing to its pharmacological properties. These bioactive compounds include alkaloids, flavonoids, terpenoids, chromenes, coumarins, and sterols, each playing distinct roles in the plant's medicinal applications.

2.2 Major Phytochemical Classes

Alkaloids

Alkaloids represent nitrogen-containing compounds with diverse biological activities. A. conyzoides contains notable alkaloids including echinatine and lycopsamine (pyrrolizidine alkaloids). These compounds demonstrate analgesic, antimicrobial, and anti-inflammatory properties [7]. However, pyrrolizidine alkaloids present hepatotoxic risks, requiring careful evaluation in therapeutic applications.

Flavonoids

Prominent flavonoids identified in A. conyzoides include kaempferol, quercetin, and quercetin-3-rhamnopyranoside. These bioactive compounds function as potent antioxidants, demonstrating anti-inflammatory, antiviral, and immunomodulatory effects [8]. Flavonoids contribute substantially to the plant's ability to reduce inflammatory responses, protect against oxidative stress, and inhibit microbial proliferation.

Terpenoids

Volatile and semi-volatile terpenoids present in A. conyzoides include α-pinene, β-pinene, and phytol. These aromatic compounds exhibit antimicrobial, anti-inflammatory, and antioxidant properties, likely accounting for a significant proportion of the plant's essential oil-derived therapeutic effects [8].

Chromenes

Precocene I and precocene II represent the major chromene compounds in A. conyzoides. These aromatic compounds demonstrate insecticidal and antimicrobial properties, supporting the plant's traditional use as a natural pesticide and antimicrobial agent [9].

Coumarins

Coumarin compounds present in A. conyzoides exhibit anticoagulant and anti-inflammatory properties. Their concentration varies based on plant part and growth conditions, contributing modestly to overall anti-inflammatory effects [8].

Sterols

Plant sterols identified in A. conyzoides include stigmasterol, β-sitosterol, and friedeline. These compounds promote cellular membrane stability and demonstrate anti-inflammatory and cholesterol-modulating properties relevant to cardiovascular health [8][10].

2.3 Quantitative Phytochemical Profile

Analysis of methanolic leaf extracts of A. conyzoides sourced from Uttar Pradesh, India, revealed the following phytochemical concentrations:

Phytochemical Class	Concentration (%)	Significance
Flavonoids	0.97-0.98	High antioxidant and anti-inflammatory potential
Saponins	0.97-0.98	Immune-modulating and hemolytic properties
Alkaloids	0.90	Analgesic and antimicrobial contributions
Tannins	0.187-0.188	Moderate astringent properties
Phenols	0.022	Lower contribution to overall antioxidant activity

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III. EXTRACTION METHODS AND PHYTOCHEMICAL ANALYSIS

3.1 Extraction Methodologies

Phytochemical extraction from A. conyzoides employs multiple techniques tailored to isolate specific compound classes from diverse plant parts (leaves, stems, flowers).

Solvent Extraction

Solvent extraction represents the most versatile and widely employed methodology. Selection of solvent based on polarity enables differential extraction of various phytochemical classes:

1. **Ethanol Extraction:** Efficiently extracts polar compounds including flavonoids and phenolic acids
2. **Methanol Extraction:** Broad-spectrum extraction of alkaloids, flavonoids, and terpenoids
3. **Acetone Extraction:** Preferential extraction of lipophilic compounds including sterols and terpenoids

Standard procedure involves soaking ground or powdered plant material in selected solvent for 14-15 days with periodic agitation. The resulting suspension is filtered, concentrated via rotary evaporation under reduced pressure, yielding crude extracts suitable for further purification or analysis.

Steam Distillation

Steam distillation specifically targets volatile essential oil components, particularly terpenoids. This method involves passing steam through plant material, condensing the resulting vapor mixture, and collecting separated essential oils. The process yields essential oils rich in therapeutic terpenoids while maintaining volatility and aromatic properties.

Supercritical Fluid Extraction (SFE)

Supercritical CO_2 extraction represents an advanced technique for isolating non-polar and semi-polar compounds. Carbon dioxide achieves supercritical properties (tunable liquid-gas behavior) at specific temperatures and pressures, providing:

- Selective extraction of target compounds without residual solvents
- Cleaner extracts suitable for pharmaceutical applications
- Superior purity and concentration of bioactive compounds
- Reduced environmental impact compared to conventional solvents

Additional Extraction Techniques

Complementary methods including maceration, Soxhlet extraction, and microwave-assisted extraction (MAE) offer flexibility in targeting specific phytochemical classes based on research objectives and extract applications.

3.2 Analytical Techniques for Phytochemical Characterization

High-Performance Liquid Chromatography (HPLC)

HPLC analysis of A. conyzoides extracts has identified and quantified multiple flavonoid classes. Okujayeet al. [11] identified kaempferol, quercetin, and quercetin glycosides, observing higher flavonoid concentrations in flower extracts compared to leaf extracts. Similarly, Cheng et al. [12] documented phenolic compounds including chlorogenic acid, caffeic acid, and ferulic acid, with leaf extracts demonstrating the highest phenolic concentrations among various plant parts.

GasChromatography MassSpectrometry (GC-MS)

GC-MS analysis has extensively profiled volatile secondary metabolites in A. conyzoides essential oils. Menut et al.[13] identified precocene I, precocene II, and ageratochromene as major essential oil constituents, with relative abundances varying based on plant geographical origin. Borah et al.[14] identified 45 distinct compounds in leaf, stem, and flower extracts, with leaf extracts demonstrating the highest compound diversity including terpenes, fatty acids, and esters.

Nuclear Magnetic Resonance (NMR) Spectroscopy

NMR spectroscopy, particularly 1D and 2D experiments, has elucidated structures of complex secondary metabolites. Ramos et al.[15] characterized chromene derivatives including ageratochromene and ageratochromene dimers, documenting antimicrobial and insecticidal properties. Srivastava et al.[16] identified pyrrolizidine alkaloid structures including echinatine and related compounds via NMR analysis.

IV. PHARMACOLOGICAL PROPERTIES AND MECHANISMS OF ACTION

4.1 Antimicrobial and Antifungal Activities

In Vitro Studies

A. conyzoides extracts demonstrate significant antimicrobial activity against diverse pathogenic bacteria and fungi. The ethanolic extract exhibits substantial inhibitory effects against:

- **Bacterial pathogens:** Staphylococcus aureus, Escherichia coli, gram-positive and gram-negative species
- **Fungal species:** Aspergillus Niger, Candida albicans, Microsporum gypseum, Trichophyton mentagrophytes

Comparative studies demonstrate that A. conyzoides exhibits superior antimicrobial activity compared to related medicinal plants including Ocimum gratissimum, particularly against S. aureus and E. coli [17][18].

Synergistic Antimicrobial Effects

Combination studies reveal synergistic antimicrobial activity when A. conyzoides extracts are combined with conventional antimicrobial agents (ciprofloxacin, ampicillin) against multidrug-resistant pathogens, suggesting potential applications in combination therapy strategies [17].

4.2 Antioxidant Activity

Radical Scavenging Mechanisms

Ethanolic and aqueous extracts of A. conyzoides leaves and flowers demonstrate significant antioxidant activity through DPPH (1,1-diphenyl-2-picryl hydrazyl) radical scavenging, primarily attributed to flavonoid and phenolic content [8][19]. Comparative analyses reveal that A. conyzoides antioxidant activity exceeds that of Ocimum sanctum and Mentha piperitaextracts [19].

Radiation Protection

A. conyzoides extracts exhibit radioprotective properties through free radical scavenging and oxidative stress reduction, demonstrating potential applications in managing radiation-induced cellular damage[8][20].

4.3 Anti-Inflammatory Activity

Hydroalcoholic leaf extracts reduce inflammatory responses in rat models, achieving 38.7% reduction in cotton pellet-induced granuloma formation[5]. In a rheumatoid arthritis rat model, A. conyzoides ethanolic extract effectively reduced paw edema, inflammatory marker levels (TNF-α), and osteoclast numbers, supporting anti-inflammatory and potential antiarthritic applications[21].

4.4 Anticancer and Cytotoxic Activities

A. conyzoides extracts demonstrate cytotoxic and antiproliferative effects against multiple cancer cell lines including breast, lung, and prostate cancer cells. These effects are attributed to bioactive compounds such as flavonoids and terpenoids, which induce apoptosis and inhibit cancer cell proliferation [8][22]. Additional studies indicate potential 5-alpha-reductase inhibition relevant to benign prostatic hypertrophy management [23].

4.5 Antidiabetic and Hepatoprotective Effects

A. conyzoides extracts modulate glucose metabolism and protect against hepatic damage, suggesting therapeutic potential in diabetes management and liver disease treatment [8][22]. These hepatoprotective effects warrant investigation given the plant's concurrent hepatotoxic alkaloid content.

4.6 Wound Healing and Gastroprotection

Leaf extracts promote wound healing through antimicrobial and anti-inflammatory mechanisms, supporting traditional wound dressing applications [24]. Additionally, gastroprotective effects against gastric ulcer formation have been documented, validating traditional gastrointestinal applications [8][21].

V. TOXICOLOGICAL ASSESSMENT AND SAFETY

Profile

5.1 Acute Toxicity Studies

Ethanolic Extract

The ethanolic extract of A. conyzoides demonstrated non-mutagenic, non-clastogenic, and non-genotoxic properties in comprehensive toxicological evaluations, indicating a favorable acute toxicity profile [25].

Essential Oil

The acute oral LD_{50} (lethal dose 50%) of A. conyzoides essential oil was determined at 1247.88 mg/kg in female mice and 1674.57 mg/kg in male mice, indicating moderate acute toxicity [19].

5.2 Subchronic Toxicity Studies

Ethanolic Extract

A 90-day repeated-dose oral toxicity study in rats established a No Observed Adverse Effect Level (NOAEL) of 2000 mg/kg body weight/day for both male and female rats. The extract produced no mortality or significant toxic changes at the highest tested dose, indicating a wide safety margin for sub-chronic exposure[25].

Essential Oil

A 28-day sub chronic toxicity study at 100 mg/kg body weight/day revealed concerning effects including:

- Decreased kidney weight and elevated serum creatinine (indicating potential renal dysfunction)
- Reduced hemoglobin, erythrocyte counts, and hematocrit values
- Gender-specific responses with more pronounced effects in male rats

These findings necessitate cautious application of A. conyzoides essential oil and further investigation of safe dosage parameters [19].

5.3 Hepatotoxicity Concerns

The pyrrolizidine alkaloid content (particularly lycopsamine and echinatine) poses hepatotoxic risks upon ingestion. These compounds are known to cause severe liver damage and potential tumor formation, necessitating careful evaluation and potential standardized extraction methods to minimize alkaloid concentration [2][6].

5.4 Safety Recommendations

- **Ethanolic Extract:** Demonstrates favorable safety profile suitable for therapeutic investigation at doses up to 2000 mg/kg bw/day in preclinical models
- **Essential Oil:** Requires cautious application due to documented renal and hematological effects at lower doses (100 mg/kg bw/day)
- **Pyrrolizidine Alkaloid Content:** Demands standardized extraction protocols minimizing hepatotoxic alkaloid concentration
- **Future Direction:** Further clinical investigations essential before widespread therapeutic implementation

VI. CLINICAL APPLICATIONS AND THERAPEUTIC POTENTIAL

6.1 Anti-Inflammatory and Analgesic Applications

A. conyzoides demonstrates clinical potential in managing inflammatory and pain-related conditions. Studies in rheumatoid arthritis models documented significant reductions in inflammatory markers, joint swelling, and disease progression, supporting further clinical investigation in human populations [21].

6.2 Antimicrobial and Antifungal Therapy

The broad-spectrum antimicrobial and antifungal activities documented in vitro suggest potential applications in managing:

1. Bacterial infections resistant to conventional antimicrobials
2. Fungal infections including Candida and Aspergillus species
3. Combination therapy approaches enhancing antimicrobial efficacy

6.3 Antioxidant and Radioprotective Therapy

Potential applications in managing oxidative stress-related pathologies and radiation-induced cellular damage represent promising therapeutic areas warranting clinical investigation [8][20].

6.4 Oncology Applications

Documented cytotoxic and antiproliferative effects against multiple cancer cell lines suggest potential contributions to anticancer therapeutic strategies, particularly when combined with conventional chemotherapeutic agents [22].

6.5 Metabolic Disorder Management

Antidiabetic and hepatoprotective properties indicate potential applications in diabetes management and liver disease treatment, though clinical evidence remains limited [8][22].

VII. LIMITATIONS AND FUTURE DIRECTIONS

7.1 Current Research Limitations

- **Limited Clinical Trials:** Majority of evidence derives from in vitro and animal model studies; human clinical trials are sparse
- **Standardization Deficiency:** Lack of standardized extraction protocols and quality control measures across studies
- **Mechanistic Gaps:** Complete molecular mechanisms underlying pharmacological activities remain inadequately characterized

- **Toxicological Uncertainties:** Pyrrolizidine alkaloid hepatotoxicity requires further investigation and mitigation strategies
- **Dose-Response Characterization:** Optimal therapeutic dosages in human populations remain undefined

7.2 Future Research Priorities

1. **Standardized Extraction Methods:** Development of validated, reproducible extraction protocols producing consistent phytochemical profiles
2. **Mechanistic Studies:** Comprehensive investigation of molecular pathways underlying pharmacological activities using proteomics, genomics, and metabolomics
3. **Clinical Trials:** Well-designed, prospective, randomized, controlled clinical trials in human populations
4. **Toxicological Research:** Advanced toxicological investigation of essential oil preparations and pyrrolizidine alkaloid mitigation strategies
5. **Formulation Development:** Development of optimized pharmaceutical formulations ensuring bioavailability and therapeutic efficacy
6. **Drug-Drug Interactions:** Investigation of potential interactions with conventional pharmaceuticals in combination therapy approaches
7. **Bioavailability Studies:** Characterization of absorption, distribution, metabolism, and excretion (ADME) properties

VIII. CONCLUSION

Ageratum conyzoides L. represents a promising medicinal plant with substantial pharmacological potential substantiated by both ethnobotanical use and contemporary scientific investigation. The comprehensive phytochemical analysis reveals a complex profile of secondary metabolites including flavonoids, alkaloids, terpenoids, chromenes, coumarins, and sterols, each contributing distinct pharmacological properties [1][8][19].

Documented pharmacologicalactivities—antimicrobial, antifungal, antioxidant, anti-inflammatory, anticancer, antidiabetic, and hepatoprotective—provide scientific validation for traditional medicinal applications while indicating potential novel therapeutic applications in modern medicine [5][8][21][22]. The synergistic effects observed in combination with conventional therapeutic agents suggest promising approaches to enhanced clinical efficacy [17][23].

However, the presence of hepatotoxic pyrrolizidine alkaloids necessitates careful evaluation and development of standardized preparation methods minimizing toxic compound concentrations. The current evidence base, while extensive, remains predominantly preclinical, highlighting the critical need for rigorous human clinical trials establishing safety parameters, optimal dosages, and therapeutic efficacy [2][25].

Future pharmaceutical development of A. conyzoides requires integration of traditional knowledge with contemporary scientific methodology, establishment of standardized quality control measures, investigation of molecular mechanisms, and comprehensive clinical evaluation. Such research could transform this ethnobotanically significant plant into a validated therapeutic agent addressing contemporary healthcare challenges in antimicrobial resistance, inflammatory diseases, and cancer management.

The multifaceted properties and relatively accessible cultivation of A. conyzoides position it favorably for development as a source of natural therapeutics within the framework of evidence-based herbal medicine and sustainable pharmaceutical development.

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