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ANDROGRAPHIS PANICULATA: A COMPREHENSIVE REVIEW OF ITS PHYTOCHEMICAL AND THERAPEUTIC POTENTIAL

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ABSTRACT

Andrographis paniculata (Burm. f.) Wall. Ex Nees, commonly known as *Kalmegha* or the "King of Bitters", is an important medicinal plant widely used in traditional systems of medicine such as Ayurveda, Siddha, and Traditional Chinese Medicine. The plant has been traditionally employed for the treatment of fever, liver disorders, infections, inflammation, and immune-related diseases. Modern pharmacological studies have validated many of these traditional claims and revealed a wide range of biological activities attributed mainly to diterpenoid lactones such as andrographolide. This review summarizes the ethnobotany, morphology, phytochemistry, and pharmacological properties of *A. paniculata* based on experimental and clinical evidence.

KEYWORDS: *Andrographis paniculata, Kalmegha,* andrographolide, Hepatoprotective activity.

1. INTRODUCTION

Medicinal plants have played a crucial role in human healthcare systems since ancient times, particularly in developing countries where traditional medicine remains the primary source of treatment [1]. *Andrographis paniculata* belongs to the family Acanthaceae and is widely distributed in India, Sri Lanka, China, and Southeast Asia [2]. In *Ayurveda*, *Kalmegh* is described as a bitter tonic and is extensively prescribed for fever (*jwara*), liver disorders, skin diseases, digestive disturbances, and infections [3,6].

The intense bitterness of the plant is attributed to diterpenoid lactones, which are also responsible for its pharmacological effects [4]. Extensive scientific research over the last few

decades has demonstrated that *A. paniculata* exhibits anti-inflammatory, antioxidant, hepatoprotective, antidiabetic, antimicrobial, antiviral, immunomodulatory and anticancer activities [5,7,8]. These findings have renewed interest in the plant as a potential source of therapeutic agents.

2. VERNACULAR NAMES (22)

Hindi	Kalamegha, Kalpanath
Bengali	Kalamegh
Malayalam	Nelavepu, Nelavemu, Nilavaepu
Telugu	Nelavemu
Kannada	Nelabevu
English	Create

3. T AXONOMICAL CLASSIFICATION (21)

Kingdom	Plantae
Phylum	Streptophyta
Class	Equisetopsida
Subclass	Magnoliidae
Order	Lamiales
Family	*Acanthaceae*
Genus	*Andrographis*
Species	*Andrographis paniculata*

4. MORPHOLOGY

Andrographis paniculata is an erect, annual herb that grows up to 30–110 cm in height [2]. The stem is slender, green, quadrangular, and highly branched. Leaves are simple, opposite, lanceolate to ovate-lanceolate, with entire margins and acute apices [9]. The flowers are small, tubular, and arranged in terminal and axillary panicles. They are pale green with purplish or violet markings [2]. The fruit is a linear-oblong capsule containing numerous yellowish-brown seeds [10]. The plant prefers tropical climates and grows well in moist and shady conditions.

Fig. *Andrographis paniculata* plant.

5. ETHNOBOTANICAL AND TRADITIONAL USES

Traditionally, *A. paniculata* has been used as a remedy for fever, malaria, jaundice, dysentery, diarrhoea, and respiratory infections [3,6]. In Ayurveda, the whole plant is used as a blood purifier, liver tonic, and digestive stimulant [1]. Tribal communities use leaf decoctions for treating intestinal worms and snake bites [9]. In Traditional Chinese Medicine, the plant is used for detoxification, treatment of sore throat, and inflammatory disorders [7]. These traditional uses have provided the basis for modern pharmacological investigations.

6. PHYTOCHEMICAL CONSTITUENTS

Phytochemical studies have revealed that *A. paniculata* contains a diverse range of secondary metabolites [4]. The major bioactive compounds are diterpenoid lactones such as andrographolide, neoandrographolide, deoxyandrographolide and 14-deoxy-11,12-didehydroandrographolide [5,10]. In addition, the plant contains flavonoids including luteolin, apigenin, and quercetin, along with polyphenols, tannins, saponins, and trace alkaloids [6,18].

Among these compounds, andrographolide is considered the principal active constituent and has been extensively studied for its pharmacological effects [7,16]. Variations in phytochemical content have been observed depending on geographical location, plant part used, and extraction method [20].

7. PHARMACOLOGICAL ACTIVITIES

7.1 Anti-inflammatory Activity

Andrographolide exhibits potent anti-inflammatory activity by inhibiting the production of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6 [8]. It suppresses the activation of NF-κB signaling pathways, thereby reducing inflammatory responses in experimental models [8,15].

7.2 Antioxidant Activity

Extracts of *A. paniculata* show significant antioxidant activity by scavenging free radicals and enhancing endogenous antioxidant enzymes such as superoxide dismutase and catalase [10,19]. The antioxidant potential is mainly attributed to flavonoids and polyphenolic compounds present in the plant [18].

7.3 Hepatoprotective Activity

Several studies have demonstrated the hepatoprotective effect of *A. paniculata* against chemically induced liver damage [11,14]. Andrographolide protects hepatocytes by reducing

oxidative stress, normalizing liver enzyme levels, and improving histopathological conditions [11].

7.4 Antidiabetic Activity

The antidiabetic activity of *A. paniculata* has been confirmed in experimental diabetic models [10]. The plant extract reduces blood glucose levels and improves insulin sensitivity by modulating carbohydrate metabolism and antioxidant defense mechanisms [10,18].

7.5 Antimicrobial and Antiviral Activity

A. paniculata exhibits broad-spectrum antimicrobial activity against various bacterial and fungal strains [6]. Andrographolide has also shown significant antiviral activity against viruses such as influenza, chikungunya, and hepatitis by inhibiting viral replication and enhancing immune responses [7,12,17].

7.6 Immunomodulatory Activity

The plant enhances immune responses by stimulating macrophage activation, lymphocyte proliferation, and antibody production [15,16]. These immunomodulatory effects support its traditional use as an immune booster [12].

7.7 Anticancer Activity

Recent studies indicate that andrographolide possesses anticancer potential by inducing apoptosis, inhibiting tumour cell proliferation, and arresting the cell cycle in various cancer cell lines [13,16]. These effects suggest its possible role as a complementary anticancer agent.

8. CLINICAL STUDIES

Clinical investigations of *Andrographis paniculata* and its major bioactive constituents have explored its therapeutic potential in a variety of infectious and inflammatory conditions. Clinical evidence has particularly focused on acute gastrointestinal infections and uncomplicated upper respiratory tract infections (URTIs), while preliminary studies have also evaluated its use in other infectious diseases.

8.1 Dysentery and Gastroenteritis

Clinical studies conducted in China have reported the therapeutic potential of *A. paniculata* in acute bacillary dysentery and acute gastroenteritis. Ethanol extract tablets of the plant were reported to produce a cure rate of 88.3% in acute bacillary dysentery and 91.3% in acute gastroenteritis.

Andrographolide, the principal diterpenoid lactone of *A. paniculata*, has also been investigated in acute bacillary dysentery. Administration of andrographolide was reported to result in a 91% cure rate. Similarly, a compound tablet containing andrographolide and

neoandrographolide in a 7:3 ratio produced a reported cure rate of 91.1% in patients with bacillary dysentery. The reported cure rate was higher than those obtained with furazolidone or chloramphenicol in the cited studies.

These findings suggest potential antimicrobial and therapeutic activity of *A. paniculata* preparations in acute gastrointestinal infections. However, interpretation of these findings should consider the limitations of the available clinical reports and differences in study methodology and preparation.[25]

8.2 Infectious Diseases

A. paniculata and its constituents have been investigated in several infectious conditions, including leptospirosis, pulmonary tuberculosis, tuberculous meningitis, and acute pyelonephritis. In cases of acute pyelonephritis, the reported therapeutic outcomes were comparable to those obtained with nitrofurantoin, with fewer adverse effects being reported in the cited study.

The plant has also been investigated in thromboangiitis obliterans. Intra-arterial or retrograde intravenous administration was reportedly associated with beneficial effects, particularly in cases described as the "heat toxic type."

Traditional formulations containing *A. paniculata* have additionally been reported in the management of snake-bite cases. In one report, ten cases of viper bite were reportedly cured within 3–5 days following administration of a compound formulation in which *A. paniculata* was the principal constituent. These findings are preliminary and should not be interpreted as establishing the plant as a substitute for established emergency management of envenomation.[25]

8.3 Clinical Investigation in HIV Infection

A Phase I dose-escalation clinical trial evaluated andrographolide in 13 HIV-positive patients and five HIV-negative healthy volunteers. The planned treatment protocol involved administration of andrographolide at 5 mg/kg body weight for the first three weeks, followed by 10 mg/kg for three weeks, and subsequently 20 mg/kg for a final three weeks.

Andrographolide administration was associated with an increase in the mean CD4+ lymphocyte count among HIV-positive patients, from a baseline mean of 405 cells/mm^3 to 501 cells/mm^3. However, no statistically significant change was observed in mean plasma HIV-1 RNA levels.

The clinical trial was discontinued after six weeks because of adverse events. Therefore, although an increase in CD4+ lymphocyte counts was observed, the available evidence was insufficient to establish the clinical efficacy of andrographolide as a treatment for HIV

infection. Further controlled clinical studies would be necessary to determine its therapeutic relevance and safety in this population.[26]

8.4 Upper Respiratory Tract Infections

Uncomplicated upper respiratory tract infections (URTIs) represent one of the most extensively investigated clinical applications of *A. paniculata*. Clinical studies have reported differences in therapeutic effectiveness depending on the type of preparation, dose, standardization, and duration of treatment.

Pills prepared from the whole powdered plant administered with water were reported to have an aggregate effectiveness rate of approximately 88%, whereas tablets prepared from an aqueous extract showed an effectiveness rate of approximately 61% in URTIs. These findings indicate that the method of preparation and the concentration of active constituents may influence clinical outcomes.[25]

In a randomized, double-blind, controlled study, 152 adults with pharyngotonsillitis received *A. paniculata* at a dose of 6 g/day for seven days. The efficacy of the treatment was reported to be comparable to acetaminophen in relieving symptoms such as fever and sore throat. Self-limiting adverse effects were reported in approximately 20% of patients in both treatment groups.[27]

Another clinical study involving 158 adults with common cold evaluated a standardized dried extract of *A. paniculata*, designated SHA-10, at a dose of 1,200 mg/day for five days. The extract significantly reduced the intensity of symptoms including tiredness, sleeplessness, sore throat, and nasal secretion, with improvements becoming evident from the second day of treatment. No significant adverse effects were reported in this study.[28]

8.5 Clinical Studies of Kan Jang

A standardized commercial preparation containing *A. paniculata* in combination with *Eleutherococcus senticosus*, marketed as Kan Jang, has been evaluated in uncomplicated URTIs.

Two randomized, double-blind, placebo-controlled parallel-group studies were conducted in Sweden. The first was a pilot study involving 46 patients, who received Kan Jang three times daily for a minimum of three days and a maximum of eight days. The second was a Phase III study involving 179 patients, with treatment administered for three days.

Clinical outcomes were assessed using patients' self-evaluation of symptoms including muscle aches, cough, sore throat, headache, nasal discharge, eye symptoms, and fever. Significant improvement in sore-throat symptoms was reported in the treatment groups compared with placebo in both studies.[29]

A similar clinical study conducted in Armenia included 95 patients with acute URTIs, including sinusitis, who received Kan Jang for five days, while 90 patients served as controls. Significant improvement was reported in headache, nasal and throat symptoms, and general malaise in the treated groups, including patients with sinusitis. However, cough and eye symptoms did not differ significantly from the placebo group.[30]

8.6 Use in Children with Respiratory Infections

The effects of Kan Jang have also been investigated in children aged 4–11 years with uncomplicated respiratory infections. In a three-arm study, one group received standard treatment, while two groups received Kan Jang or an *Echinacea* preparation as an adjunct to standard therapy for ten days.

Children who received Kan Jang as an adjunct to standard treatment at an early stage of the common cold experienced less severe symptoms, particularly nasal congestion and nasal secretion. They also showed faster recovery and a significantly lower requirement for standard medication.[31]

8.7 Evidence from Systematic Reviews

Two systematic reviews of randomized controlled trials concluded that *A. paniculata* appeared to be a safe and efficacious alternative treatment for uncomplicated URTIs when compared with placebo. The available evidence therefore provides comparatively stronger clinical support for its use in uncomplicated upper respiratory infections than for several other therapeutic indications.

However, an important limitation is that the results of the Kan Jang trials cannot be attributed exclusively to *A. paniculata*, because the preparation also contains *Eleutherococcus senticosus*. Consequently, the individual contribution of *A. paniculata* to the observed therapeutic effects cannot be determined with certainty from these studies.

Furthermore, many other clinical trials involving *A. paniculata* have been published in Chinese journals and lack sufficient methodological details to allow reliable assessment of their efficacy. Some of the conditions investigated are also self-limiting, which makes interpretation of treatment effects difficult. [32,33]

8.8 Overall Clinical Perspective

Overall, clinical evidence indicates that *A. paniculata* has promising therapeutic potential, particularly in uncomplicated upper respiratory tract infections, with additional preliminary evidence in acute bacillary dysentery and gastroenteritis. The clinical response appears to depend on the plant preparation, extraction method, standardization, dosage, and duration of treatment.

Nevertheless, evidence for several other infectious and systemic conditions remains limited. Further well-designed, adequately powered, randomized controlled clinical trials using standardized *A. paniculata* preparations are required to establish its efficacy, optimal dosage, safety profile, and specific therapeutic indications.

9 TOXICITY, SAFETY PROFILE

The safety profile of *Andrographis paniculata* and its major bioactive constituent, andrographolide, has been investigated in experimental and clinical studies. The reported median lethal dose (LD_{50}) of the alcohol extract of *A. paniculata*, obtained by cold maceration, was found to be 1.8 g/kg in experimental animals. The LD_{50} of andrographolide, which constituted approximately 0.78% w/w of the whole plant, was reported to be 11.46 g/kg following intraperitoneal administration in male mice. These findings indicate a relatively wide safety margin in experimental conditions; however, the safety profile may vary depending on the preparation, dose, route of administration, and duration of exposure.

Clinical safety data have also been reported. In a study involving HIV-positive patients, a daily dose of 1,500–2,000 mg of andrographolides was administered for six weeks. Although some improvement in CD4+ cell counts was observed, adverse effects were commonly reported and the study was discontinued prematurely. This finding highlights the importance of appropriate dose selection and careful monitoring during prolonged or high-dose administration.

The safety of *A. paniculata* during pregnancy and conception remains insufficiently established. In the absence of definitive evidence regarding its effects on reproduction and fetal development, precautionary use is recommended. Therefore, until adequate reproductive safety data are available, the use of *A. paniculata* should preferably be avoided during attempts at conception and during pregnancy. [23,24]

8. CONCLUSION

Andrographis paniculata is a medicinally valuable plant with extensive traditional use and strong pharmacological validation. Its diverse biological activities are mainly attributed to diterpenoid lactones, particularly andrographolide. The scientific evidence summarized in this review supports the therapeutic potential of *A. paniculata* and highlights the need for further clinical studies to establish its safety, efficacy, and molecular mechanisms. The plant represents a promising natural source for future drug development.

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