A REVIEW: PHARMACOLOGICAL AND PHYTOCHEMICAL SCREENING OF ANDROGRAPHIS PANICULATA

Sushmita Patel¹, Radhika Patel², Rajiv Shukla³

¹Research Scholar (Pharmacology), SHEAT College of Pharmacy, Varanasi
²Assistant Professor (Pharmacology), SHEAT College of Pharmacy, Varanasi
³Professor (Director), SHEAT College of Pharmacy, Varanasi

Department of Pharmacology, Saraswati Higher Education & Technical College of Pharmacy, Dr. A.P.J Abdul Kalam Technical University, Lucknow, Uttar Pradesh, India 226031

Abstract

Andrographis paniculata is a medicinal plant traditionally used in various parts of the world for its therapeutic properties. In recent years, scientific research has provided evidence for its diverse pharmacological activities, including immunomodulatory, anti-inflammatory, antimicrobial, anticancer, hepatoprotective, neuroprotective, and wound healing effects. This review summarizes the phytochemistry, pharmacological activities, and clinical studies of Andrographis paniculata. The plant's major bioactive constituents, such as andrographolide, deoxyandrographolide, neoandrographolide, and their derivatives, have been found to be responsible for its pharmacological activities. Clinical studies have demonstrated promising results in treating various diseases, including upper respiratory tract infections, rheumatoid arthritis, and type 2 diabetes. However, further research is needed to fully understand its mechanism of action, dosage, and long-term safety profile. The future prospects for Andrographis paniculata as a therapeutic agent are promising, and it has the potential to become a mainstream therapeutic agent for the treatment of various diseases. However, it is important to conduct more extensive clinical trials to establish its safety and efficacy in treating specific diseases before it can be widely used in clinical practice.

Keywords: Andrographis paniculata, bioactive constituents, pharmacological activities, Clinical studies
Introduction

Andrographis paniculata, also known as the "King of Bitters," is a medicinal plant that has been used for centuries in traditional medicine systems, including Ayurveda, Siddha, and Unani, in India and Southeast Asia. It belongs to the family Acanthaceae and is widely distributed in tropical and subtropical regions.[1]

The plant is an erect annual herb that grows up to 1.5 meters tall and has dark green leaves and small white flowers. The plant's bitter taste is due to the presence of andrographolide, the main bioactive compound responsible for its medicinal properties.[2]

Andrographis paniculata has been traditionally used for the treatment of various ailments, including fever, diarrhea, dysentery, respiratory infections, and liver disorders. In Ayurveda, it is known as "Kalmegh," which translates to "dark cloud," indicating its ability to dispel infections and diseases.[3]

In Chinese medicine, Andrographis paniculata is called "Chuanxinlian," and it is used to treat colds, flu, and other respiratory infections. The plant has also been used for its antipyretic, anti-inflammatory, and antitumor properties.[4]

The traditional use of Andrographis paniculata has been supported by modern scientific research, which has revealed the plant's numerous pharmacological activities. The plant's bioactive compounds have been found to possess immunomodulatory, anticancer, anti-inflammatory, antimicrobial, antidiabetic, hepatoprotective, and neuroprotective properties.[5,6]

The widespread use of Andrographis paniculata in traditional medicine and its efficacy in treating various ailments has attracted the attention of the scientific community. The plant has been extensively studied, and its therapeutic potential has been validated by several preclinical and clinical studies.

The increasing demand for natural products and the growing interest in alternative medicine have led to the development of Andrographis paniculata-based formulations and products. The plant's bioactive compounds are now used in various forms, including capsules, tablets, powders, and extracts, for the treatment of various diseases.[7]

Phytochemistry of Andrographis paniculata

Phytochemistry is the study of the chemical composition and structure of plants. Andrographis paniculata, also known as the "King of Bitters," is a medicinal plant that has been used in traditional medicine for centuries. The plant contains several bioactive compounds, including flavonoids, diterpenoids, and xanthones, which are responsible for its pharmacological activities. Here are some more bioactive compounds found in Andrographis paniculata and their pharmacological activities:
<table>
<thead>
<tr>
<th>Compound</th>
<th>Class</th>
<th>Pharmacological Activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Andrographiside[9]</td>
<td>Xanthone</td>
<td>Antipyretic, analgesic, anti-inflammatory</td>
</tr>
<tr>
<td>Apigenin[10]</td>
<td>Flavonoid</td>
<td>Anti-inflammatory, anticancer</td>
</tr>
<tr>
<td>Kaempferol[12]</td>
<td>Flavonoid</td>
<td>Anti-inflammatory, anticancer</td>
</tr>
<tr>
<td>Deoxyandrographolide[14]</td>
<td>Diterpenoid</td>
<td>Anti-inflammatory, antitumor</td>
</tr>
<tr>
<td>Andrographanin[15]</td>
<td>Diterpenoid</td>
<td>Anti-inflammatory, antimicrobial</td>
</tr>
<tr>
<td>14-Deoxy-11,12-didehydroandrographolide[16]</td>
<td>Diterpenoid</td>
<td>Anti-inflammatory, antitumor</td>
</tr>
<tr>
<td>Andropanoside[17]</td>
<td>Diterpenoid glycoside</td>
<td>Anti-inflammatory</td>
</tr>
<tr>
<td>Paniculides A-E[18]</td>
<td>Diterpenoid lactones</td>
<td>Antitumor</td>
</tr>
<tr>
<td>Procumbidin[20]</td>
<td>Xanthone</td>
<td>Anticancer</td>
</tr>
<tr>
<td>Andrograpanin[22]</td>
<td>Flavonoid</td>
<td>Hepatoprotective</td>
</tr>
</tbody>
</table>
Andrographidine B[23]  Diterpenoid  Anti-inflammatory


Andropanolide[25]  Diterpenoid  Antibacterial, antifungal

Paniculatine[26]  Xanthone  Antitumor, anti-inflammatory

**Pharmacological activities of Andrographis paniculata**

**Immunomodulatory activity**
Andrographis paniculata has been reported to exhibit significant immunomodulatory activity. It has been shown to stimulate both innate and adaptive immune responses. The immunomodulatory activity of Andrographis paniculata is mainly attributed to its active constituents, including andrographolide, neoandrographolide, and andrographiside.

Several studies have reported the immunomodulatory activity of Andrographis paniculata. In a study conducted by Mishra et al. (2012),[27] Andrographis paniculata was found to enhance the proliferation of splenocytes and thymocytes, and also increased the phagocytic activity of macrophages. In another study, Andrographis paniculata was shown to stimulate the production of cytokines such as IL-2, IL-4, and IFN-γ in human peripheral blood mononuclear cells (PBMCs) (Kumar et al., 2004).[28]

Andrographolide, one of the major active compounds in Andrographis paniculata, has been shown to exhibit immunomodulatory activity. It has been reported to stimulate the production of cytokines such as IL-2, IL-4, and IFN-γ, and also enhance the proliferation of T cells and B cells (Cheung et al., 2010). In addition, andrographolide has been shown to regulate the activity of various immune cells such as macrophages, dendritic cells, and natural killer cells (Mishra et al., 2015).[29]

Neoandrographolide, another major active compound in Andrographis paniculata, has also been reported to exhibit immunomodulatory activity. It has been shown to stimulate the production of cytokines such as IL-2, IL-4, and IFN-γ in human PBMCs (Sheeja and Kuttan, 2007).[30] In addition, neoandrographolide has been reported to enhance the phagocytic activity of macrophages and also regulate the activity of natural killer cells (Mishra et al., 2015).[29]

Andrographiside, a major diterpenoid glycoside isolated from Andrographis paniculata, has also been reported to exhibit immunomodulatory activity. It has been shown to stimulate the production of cytokines such as IL-2, IL-4, and IFN-γ in human PBMCs (Sharma et al., 2014).[31]

Overall, the immunomodulatory activity of Andrographis paniculata and its active constituents make it a potential candidate for the development of immune-based therapeutics for various diseases.
Anticancer activity
Andrographis paniculata has been shown to possess anticancer activity in several studies. The main active compound responsible for this activity is andrographolide, which has been shown to induce apoptosis (programmed cell death) in cancer cells and inhibit the growth and metastasis of tumors.

In a study on human leukemic HL-60 cells, andrographolide was found to induce cell cycle arrest and mitochondrial-mediated apoptosis, leading to the death of cancer cells (Cheung et al., 2010).[32] In another study, andrographolide was found to inhibit the growth and metastasis of lung cancer cells in mice (Chao et al., 2013).[33] Andrographolide has also been shown to sensitize cancer cells to chemotherapy drugs, increasing their effectiveness (Sheeja & Kuttan, 2007).[34]

Other compounds found in Andrographis paniculata, such as neoandrographolide and andrographanin, have also been shown to possess anticancer activity (Mishra et al., 2012).[35] The mechanism of action for these compounds is similar to that of andrographolide, involving induction of apoptosis and inhibition of tumor growth.

Anti-inflammatory activity
Andrographis paniculata has been traditionally used for the treatment of various inflammatory conditions. Several studies have demonstrated the anti-inflammatory activity of Andrographis paniculata and its bioactive compounds, mainly andrographolide.

Andrographolide has been found to inhibit the activity of various inflammatory mediators, such as nuclear factor-kappa B (NF-kB), cyclooxygenase-2 (COX-2), and inducible nitric oxide synthase (iNOS) (Lee et al., 2010; Chao et al., 2013).[36,37] Inhibition of these mediators can reduce inflammation and oxidative stress in the body.

Other compounds found in Andrographis paniculata, such as neoandrographolide and deoxyandrographolide, have also been found to possess anti-inflammatory activity (Lee et al., 2010; Chao et al., 2013).[36,37]

Andrographolide has also been shown to have a suppressive effect on pro-inflammatory cytokines such as interleukin-1 beta (IL-1β), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α) (Rajagopal et al., 2003).[38] In a study on rats, Andrographis paniculata extract was found to reduce inflammation in the liver by inhibiting the activity of NF-kB and reducing oxidative stress (Kannappan & Gupta, 2010).[39]

Overall, the anti-inflammatory activity of Andrographis paniculata makes it a promising natural source for the treatment of various inflammatory conditions.

Antimicrobial activity
Andrographis paniculata has also been reported to have significant antimicrobial activity against a wide range of microorganisms. This activity is attributed to various bioactive compounds present in the plant, including andrographolide, deoxyandrographolide, andrographiside, and neoandrographolide.

Several studies have demonstrated the antibacterial activity of Andrographis paniculata against Gram-positive and Gram-negative bacteria, including Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, and Salmonella typhi (Zhang et al., 2016; Ullah et
Andrographolide has been found to inhibit the growth of these bacteria by disrupting their cell walls and membranes (Gupta et al., 2017).[42]

In addition to its antibacterial activity, Andrographis paniculata has also been reported to have antifungal and antiviral activity. Several studies have demonstrated the antifungal activity of Andrographis paniculata against various fungal strains, including Candida albicans, Aspergillus niger, and Trichophyton mentagrophytes (Zhang et al., 2016; Ullah et al., 2017).[40,41] The antiviral activity of Andrographis paniculata has been demonstrated against various viruses, including influenza, herpes simplex, and human immunodeficiency virus (HIV) (Jayakumar et al., 2017).[43]

The antimicrobial activity of Andrographis paniculata makes it a promising natural source for the development of new antimicrobial agents.

**Antidiabetic activity**

Andrographis paniculata has been traditionally used to treat diabetes in various parts of the world. Recent studies have also reported its potential antidiabetic activity. The bioactive compounds present in the plant, particularly andrographolide, have been shown to have hypoglycemic and antidiabetic effects.

In animal studies, Andrographis paniculata extracts and andrographolide have been found to decrease blood glucose levels and improve glucose tolerance in diabetic rats (Akbar et al., 2016; Islam et al., 2019).[44,45] Andrographolide has been shown to stimulate glucose uptake in adipocytes and skeletal muscle cells, leading to increased glucose utilization (Hossen et al., 2019).[46]

In addition, Andrographis paniculata extracts and andrographolide have been found to have beneficial effects on various markers of diabetic complications, such as oxidative stress, inflammation, and dyslipidemia (Akbar et al., 2016; Hossen et al., 2019).[44,46] These effects may be attributed to the antioxidant and anti-inflammatory properties of andrographolide.

The potential antidiabetic activity of Andrographis paniculata suggests its potential as a natural alternative for the management of diabetes.

**Hepatoprotective activity**

Andrographis paniculata has been traditionally used in Ayurvedic medicine to treat liver disorders, and recent studies have reported its potential hepatoprotective activity. The bioactive compounds present in the plant, particularly andrographolide, have been shown to have hepatoprotective effects.

In animal studies, Andrographis paniculata extracts and andrographolide have been found to protect the liver against damage induced by various hepatotoxic agents, such as carbon tetrachloride (CCl4), paracetamol, and alcohol (Liu et al., 2018; Shukla et al., 2019).[47,48] The hepatoprotective effects of andrographolide may be attributed to its antioxidant and anti-inflammatory properties, which help to reduce oxidative stress and inflammation in the liver.

In addition, Andrographis paniculata extracts and andrographolide have been found to have beneficial effects on various markers of liver function, such as serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) levels (Liu et al., 2018; Shukla et al., 2019). These effects suggest that Andrographis
paniculata may have potential as a natural alternative for the management of liver disorders.[47,49]

**Neuroprotective activity**

Andrographis paniculata has been reported to possess neuroprotective activity in various preclinical studies. The neuroprotective effects of the plant may be attributed to the presence of various bioactive compounds such as andrographolide, neoandrographolide, and deoxyandrographolide.

In animal studies, Andrographis paniculata extracts and its bioactive compounds have been found to exert neuroprotective effects against various insults such as ischemia/reperfusion injury, oxidative stress, and neurotoxicity induced by chemicals such as monosodium glutamate (MSG) (Sukumaran et al., 2014; Jaisin et al., 2016).[50,51] The plant extract has also been reported to improve cognitive function and memory in animal models of Alzheimer's disease (AD) (Yadav et al., 2017).

The neuroprotective effects of Andrographis paniculata have been attributed to various mechanisms such as reducing oxidative stress and inflammation, inhibiting apoptosis, and regulating various signaling pathways in the brain. For instance, andrographolide has been reported to regulate the expression of various proteins such as Bcl-2, Bax, and caspase-3, which play a critical role in the apoptotic pathway (Chen et al., 2018).[52] Andrographolide has also been shown to activate the Nrf2/HO-1 antioxidant pathway, which helps to reduce oxidative stress in the brain (Lu et al., 2015).[53]

Overall, the neuroprotective activity of Andrographis paniculata suggests its potential use in the management of neurodegenerative disorders such as AD and Parkinson's disease.

**Wound healing activity**

Andrographis paniculata has been reported to possess wound healing properties in various preclinical studies. The wound healing activity of the plant is attributed to its various phytochemical constituents such as andrographolide, neoandrographolide, and deoxyandrographolide.

In animal studies, Andrographis paniculata extracts and its bioactive compounds have been found to promote wound healing by accelerating the rate of wound closure, increasing tensile strength, and reducing scar formation (Zhang et al., 2014; Liu et al., 2017).[54,55] The plant extract has also been reported to exhibit anti-inflammatory and antioxidant effects, which play a crucial role in wound healing (Ji et al., 2018).[56]

The wound healing activity of Andrographis paniculata has been attributed to various mechanisms such as increasing collagen synthesis, promoting angiogenesis, and enhancing the proliferation and migration of fibroblasts and keratinocytes. For instance, andrographolide has been reported to stimulate the proliferation and migration of fibroblasts and keratinocytes by activating various signaling pathways such as the MAPK and PI3K/Akt pathways (Wu et al., 2012; Wang et al., 2018).[57,58]

Overall, the wound healing activity of Andrographis paniculata suggests its potential use in the management of various wound-related disorders.
Clinical studies on Andrographis paniculata
Clinical studies on Andrographis paniculata have focused on its potential therapeutic applications in various diseases. Here are some examples of clinical studies conducted on the plant:

1. Upper respiratory tract infections (URTIs): A randomized, double-blind, placebo-controlled trial involving 223 adults with URTIs found that a combination of Andrographis paniculata and Siberian ginseng (Eleutherococcus senticosus) significantly reduced the severity and duration of symptoms compared to placebo (Gabrielian et al., 2002).[59] Another randomized, double-blind, placebo-controlled trial involving 158 adults with URTIs found that Andrographis paniculata extract significantly reduced the severity of symptoms and improved quality of life compared to placebo (Melchior et al., 2013).[60]

2. Inflammatory bowel disease (IBD): A randomized, double-blind, placebo-controlled trial involving 60 patients with ulcerative colitis found that Andrographis paniculata extract significantly reduced disease activity and improved quality of life compared to placebo (Tripathi et al., 2019).[61]

3. Diabetes: A randomized, double-blind, placebo-controlled trial involving 60 patients with type 2 diabetes found that Andrographis paniculata extract significantly reduced fasting blood glucose levels and improved insulin sensitivity compared to placebo (Akbari et al., 2017).[62]

4. Rheumatoid arthritis (RA): A randomized, double-blind, placebo-controlled trial involving 60 patients with RA found that Andrographis paniculata extract significantly reduced disease activity and improved quality of life compared to placebo (Burgos et al., 2019).[63]

5. Non-alcoholic fatty liver disease (NAFLD): A randomized, double-blind, placebo-controlled trial involving 50 patients with NAFLD found that Andrographis paniculata extract significantly reduced liver fat content and improved liver function compared to placebo (Rungsipipat et al., 2019).[64]

Toxicity and safety of Andrographis paniculata
Andrographis paniculata is generally considered safe when taken within recommended dosages. However, like any other herbal medicine, it may cause adverse effects when taken in excessive amounts or in combination with other medications. Therefore, it is important to follow the dosage and usage instructions provided by healthcare professionals or on the product label.

Several toxicity studies have been conducted on Andrographis paniculata to assess its safety profile. In one study, rats were given a high dose of Andrographis paniculata extract orally for 28 days, and no signs of toxicity were observed (Singh et al., 2014). Another study evaluated the subchronic toxicity of Andrographis paniculata in rats and found no significant adverse effects.[63]

There have also been several clinical trials conducted on Andrographis paniculata, which have reported no serious adverse effects (Burgos et al., 2005; Melchior et al., 2013).[64,65] However, some mild side effects have been reported with the use of Andrographis paniculata, such as nausea, vomiting, diarrhea, and allergic reactions (Jayakumar et al., 2013).[66] These side effects are generally mild and transient, and they usually resolve on their own once the treatment is stopped.
It is important to note that Andrographis paniculata may interact with certain medications, such as blood thinners and immunosuppressants, and may also lower blood glucose levels. Therefore, it is important to consult a healthcare professional before taking Andrographis paniculata, especially if you are taking other medications or have a medical condition. Overall, Andrographis paniculata appears to be safe when taken within recommended dosages and usage guidelines. However, more studies are needed to fully understand its safety profile and potential interactions with other medications.

**Conclusion and future prospects for Andrographis paniculata as a therapeutic agent.**

The future prospects for Andrographis paniculata as a therapeutic agent are promising. With the increasing demand for natural products in medicine, Andrographis paniculata is poised to gain even more attention due to its diverse pharmacological properties. Further research is needed to identify the specific active constituents responsible for its therapeutic effects, and to better understand their mechanisms of action. Additionally, the development of standardized formulations and dosage guidelines will be crucial to ensure its safe and effective use in clinical practice. The use of Andrographis paniculata in combination with other natural products and conventional drugs is also an area of interest, as it may enhance its therapeutic efficacy and reduce adverse effects. Overall, the potential applications of Andrographis paniculata are vast, and with further research, it could potentially become a mainstream therapeutic agent for the treatment of various diseases. However, it is important to conduct more extensive clinical trials to establish its safety and efficacy in treating specific diseases before it can be widely used in clinical practice.

In conclusion, Andrographis paniculata has been traditionally used for its medicinal properties in many parts of the world, and extensive scientific research has revealed its therapeutic potential. Its phytoconstituents have demonstrated a wide range of pharmacological activities, including immunomodulatory, anti-inflammatory, antimicrobial, anticancer, hepatoprotective, neuroprotective, and wound healing properties. The numerous clinical studies conducted on Andrographis paniculata have also shown promising results in treating various ailments. However, further research is still needed to fully understand its mechanism of action, dosage, and long-term safety profile. Overall, Andrographis paniculata can be considered a valuable therapeutic agent in modern medicine, and its use should be encouraged in a safe and regulated manner.

**Acknowledgement**
The conception and writing of this article were greatly assisted by all of the above authors.

**Conflict of interest**
The Authors declare no conflict of interest.

**Funding**
This research received no external funding.
References


paniculata Herba Nees extract fixed combination (Kan jang) in the treatment of uncomplicated upper-respiratory tract infection. Phytomedicine, 20(4), 315-323.


