



A REVIEW OF PHYTOCONSTITUENTS AND THEIR PHARMACOLOGICAL PROPERTIES OF *ANDROGRAPHIS PANICULATA* (NEES)

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ABSTRACT

Medicines in India are used by about 60 per cent of the world's population. Traditional medicines are not only used for primary health care not just in rural areas in developing countries, but also in developed countries as well where modern medicines are predominantly used. While the traditional medicines are derived from medicinal plants, minerals, and organic matter, the herbal drugs are prepared from medicinal plants only. Since many diseases commonly treated with *Andrographis paniculata* in traditional medical system and are consider self limiting. The major objective of this review is providing a link among researchers working in a several disciplines associated with medicinal plants. This review paper also highlighted on evaluation and characterization of various bioactive phytoconstituents against various diseases based on their traditional asserts of the plants given in Ayurveda. In this review the *Andrographis paniculata* reported as having antimicrobial, anti bacterial, anti HIV, anti cancerous, hepatoprotective activity, anti diabetic, antioxidant activity etc.

KEYWORDS: *Andrographolide, anti-HIV, anti-cancerous, hepatoprotective.*



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INTRODUCTION

Nature has been a source of medicinal agents for thousands of years and since the beginning of mankind. The application of medicinal plants especially in traditional medicine is currently well acknowledged and established as a viable profession. Traditional medicine is not only used for primary health care not just in rural areas in developing countries, but also in developed countries as well where modern medicines are predominantly used. While the traditional medicines are derived from medicinal plants, minerals, and organic matter, the herbal drugs are prepared from medicinal plants only. Medicinal plants are an important source for the therapeutic remedies of various ailments. In rural India, 70 per cent of the population depends on the traditional type of medicine. There is a growing interest in correlating the Phytochemicals constituents of a medicinal plant with its pharmacological activity.

ANDROGRAPHIS PANICULATA

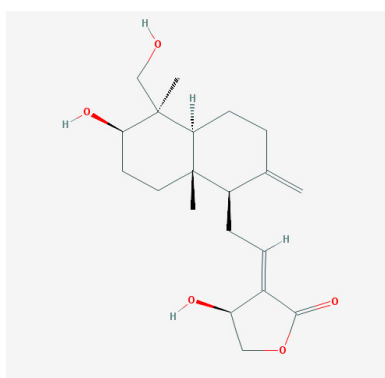
Andrographis paniculata Nees (Acanthaceae) commonly known as “king of bitter” is perennial herb widely cultivated in china, South Asia, South Africa, India Pakistan and Shri lanka. Mostly the roots and leaves have been traditionally used over the centuries for different medicinal purposes in Asia as a folklore

remedy for a wide spectrum of ailments or as an herbal supplement for health promotion.¹ In recent year, a medicinal plant *Andrographis paniculata* and its major active phytochemicals have been extensively studied for several pharmacological activities.² The Indian pharmacopoeias narrates that it is predominant constituent of at least 26 Ayurvedic.³⁻⁴

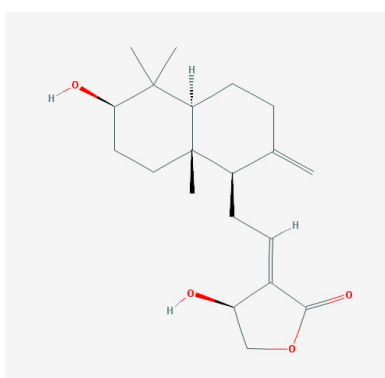
TRADITIONAL USES

ANDROGRAPHIS PANICULATA

A.paniculata was screened for various constituents (andrographolide, flavones, lactones) using routine chemical identification methods. Andrographolide is the main constituent and it also active principle of the plant: The diterpenes, lactones, and flavonoids.⁵ Flavonoids mainly exist in the root, but have also been isolated from the leaves. The aerial parts contain alkanes, ketones, and aldehydes. Although it was initially thought that the bitter substance in the leaves was the lactone andrographolide, later investigations showed that the leaves contained two bitter principles – andrographolide and a compound named kalmeghin. Four lactones chuanxinlian A (deoxy andrographolide), B (andrographolide), C (neo andrographolide) and D (14-deoxy-11, 12-didehydroandrographolide) – were isolated from the aerial parts in China (Fig 1).⁶⁻⁷

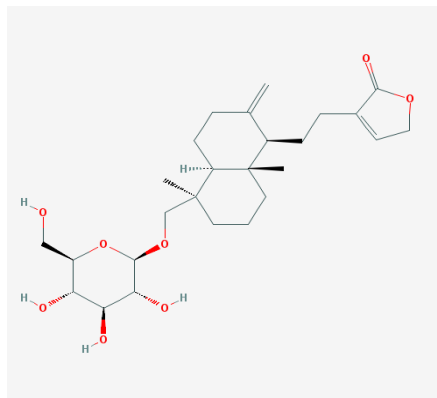
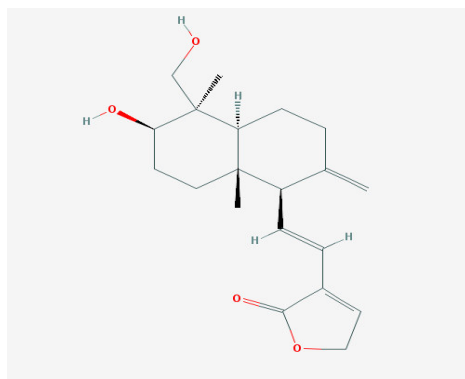


(A) Andrographolide



(B) Deoxyandrographolide

Figure 1
Structure of Phytoconstituents of *A. paniculata*

(C) *Neoandrographolide*(D) *14-deoxy-11,12-didehydroandrographolide*

A diterpene glucoside deoxyandrographolide- 19 beta-D-glucoside) has been detected in the leaves and six diterpenoids of the ent-labdane type, two diterpene glucosides and four diterpene dimers (bis-andrographolides A, B, C, and D) have been isolated from aerial parts.¹¹⁻¹² Two flavonoids identified as 5,7,2',3'-tetramethoxyflavanone and 5-hydroxy-7,2',3'-methoxyflavone were isolated from the whole plant while 12 new flavonoids and 14 diterpenoids have been reported from the aerial parts.¹³⁻¹⁴ Two new flavonoid glycosides and a new diterpenoid (andrographic acid) were recently reported, and two new ent-labdane diterpenoid glycosides were isolated from the aerial parts.¹⁵ Methanolic extract of *A. paniculata* whole plant extract contains different types of phytochemical like flavonoids, tannins, fatty acids, steroids, saponins, anthocyanins, leucoanthocyanins, coumarins, emodins, and phenols which has been shown to possess antibacterial properties against laboratory test organisms like *Staphylococcus aureus*, *Lactobacillus*, *Pseudomonas putida*, *Bacillus subtilis* and *E. coli* of bacteria.¹⁶⁻¹⁷ Traditionally in India the *Andrographis paniculata* is used for the treatment of various disease i.e. Diabetes, Disentry, Enteritis, Helminth Infection, Herpes, Peptic fever, Snake bite, Skin Infection.¹⁸ In China the traditionally used medicine is known as Chuan-Xin – Lian, Chunlianquialio, Si-Fang_Lian and is used for Fever, Common Cold, Tonsillitis, Laryngitis, Respiratory Infection.¹⁹ In the Thia medicinal system, its native name Fah-Tha-Lai, Nam Rai is reported effective against Fever, Common Cold, Non Infectious Diarrhoea.²⁰ In japan the herb derived from leaves is known as Senshinren is used for Fever, Common Cold.²¹

MAJOR RESEARCH

PHAMACOLOGICAL

HEPATOPROTECTIVE ACTIVITY.

Liver diseases of various origins remain a serious health problem and a major cause of mortality. In the absence of reliable hepatoprotective drugs in modern medicine, herbs and plants play a vital role in managing several liver disorders and also used as an ingredient in polyherbal preparations for the treatment of hepatic disorder in Ayurvedic and Unani medicinal System.²² In a comparative study, the leaf extract and andrographolide was tested against the carbon tetrachloride (CCl₄-) induced hepatic microsomal lipid peroxidation. Only the leaf extract completely protected the high concentration CCl₄-induced microsomal lipid peroxidation *in vitro* but not the andrographolide, which indicated that the hepatoprotective role is not solely due to the presence of andrographolide.²³ Andrographolide exhibits protective effects in carbon tetrachloride induced hepatopathy in rats.²⁴ Hepatoprotective effect of andrographolide against hexachlorocyclohexane-induced oxidative injury in mice model has been established.²⁵⁻²⁶ The researchers concluded that plant was a useful remedy for treatment of chronic hepatitis B virus infection.²⁷

ANTI VIRAL ACTIVITY

The antiviral activities of plant extracts have been transformed and have been the topic of keen scientific investigation. Several medicinal plant extracts have shown antiviral activities against some RNA and DNA viruses. Among these plants is *A. paniculata* which

exhibits a neutralizing activity against the human immunodeficiency virus (HIV). The hot aqueous aerial parts extract of AP was reported for its significant antiviral activity to reduce the percentage of HIV antigen-positive H9 cells.²⁸ Andrographolide was investigated for antiviral activity against herpes simplex virus (HSV), flaviviruses, and pestiviruses.²⁹⁻³¹ Recently, reported that the methanol extract of AP possesses significant inhibition activity against DENV-1 *in vitro* assay. Another study has revealed that andrographolide suppressed HPV16 transcription activity, leading to the reduction of E6 oncoprotein and restored p53.³²⁻³³

ANTI CANCER ACTIVITY

Andrographolide exhibited potent cyto-toxic activity against KB (human epidermoid leukemia) and P388 (lymphocytic leukemia) cells.²⁰ Among the diterpenoid lactones isolated from the ethyl acetate fraction of *A. paniculata*, andrographolide had strong anticancer activity by inducing cell differentiation in mouse myeloid leukemia cells.¹² Andrographolide was found to inhibit the proliferation of various cell lines including leukemia, breast cancer, lung cancer, and melanoma cells.³⁴ Furthermore, this compound has strong anticancer activity against human colorectal carcinoma LoVo cells by inhibiting cell cycle progression.³⁵ A recent study demonstrated that andrographolide inhibits breast cancer cell proliferation, migration, and cell cycle arrest at the G2/M phase and induces apoptosis through a caspase-independent pathway. Their experimental evidence suggests that andrographolide attenuates endothelial cell motility and tumor-endothelial cell interaction.³⁶

ANTI DIABETIC ACTIVITY

Orally administered glucose-induced hyperglycemia in nondiabetic rabbits was reported to be prevented by the extract of *A. paniculata*. Six weeks of chronic administration of the extract showed no effect on fasting blood glucose levels. The ethanolic extract of *A. paniculata* at a dose of 400 mg/kg body weight twice daily for 2 weeks to diabetic rats was shown to produce a 49.8% reduction in fasting serum triglyceride levels. This was reported to be greater than the 27.7% decline that was achieved with 500 mg/kg body weight twice daily for 14 days.³⁷ An aqueous extract (50 mg/kg body weight) administered to streptozotocin-diabetic rats resulted in a 52.9% reduction in blood glucose levels. Dry powder of the plant material significantly decreased blood glucose levels by 61.8% at a lower dose of 6.25 mg/kg body weight.³⁸⁻⁴⁰

ANTI OXIDANT RESISTANCE

Several studies have reported the antioxidant activities of *A. paniculata* and its constituents. The aqueous extract of *A. paniculata* significantly increased the activities of antioxidant defense enzymes such as catalase, superoxide dismutase, and glutathione-S-transferase and reduced glutathione content. The extract significantly inhibits lipid per oxidation by lowering the levels of thiobarbituric-acid-reactive substances in the liver and kidney of diabetic rats (as compared to normal rats) and also significantly increases the level of hepatic glutathione concentrations.⁴¹ Excessive amounts of NO and

prostaglandin E2 (PGE2), due to expression of inducible isoforms of nitric oxide synthase (iNOS) and cyclooxygenase-2(COX-2) from activated macrophages, play a significant role in inflammatory processes. Lipopolysaccharide (LPS) stimulates and promotes secretion of pro-inflammatory cytokines from macrophages and causes induction of iNOS, resulting in increased production of NO. Incubation of macrophages with methanol extract, andrographolide, and neoandrographolide inhibits LPS-stimulated NO production in a concentration dependent manner.⁴²⁻⁴³ Andrographolide exhibited free radical-scavenging ability, thus reduced oxidative stress and thiobarbituric-acid-reactive substance formation.⁴⁴ A key modern use of *A. paniculata* is for the prevention and treatment of the common cold. It appears to have antithrombotic actions, suggesting a possible benefit in cardiovascular disease.⁴⁵ Pharmacological and clinical studies suggest that it is beneficial effects in diseases like cancer and HIV infections.⁴⁶⁻⁴⁷

ANTI MICROBIAL ACTIVITY

Andrographis paniculata has been extensively used to treat a variety of conditions of infectious origin in traditional systems of medicine. Crude powder suspended in water was reported to be devoid of *in vitro* antibacterial activity against *Salmonella*, *Shigella*, *Escherichia coli*, gram A Streptococci, and *Staphylococcus aureus*, even at a concentration of 25mg/mL crude powder.⁴⁸ A similar conclusion was obtained when crude aqueous extract of leaves exhibit significant antimicrobial activity against grampositive *S. aureus*, methicillin-resistant *S. aureus* (MRSA), and gram-negative *Pseudomonas aeruginosa*, but had no activity against *Escherichia coli* or *Klebsiella pneumoniae*.⁴⁹ Antibacterial activity of aqueous methanol (50%v/v) crude extracts of whole plant against *Bacillus subtilis* and *Proteus vulgaris*.⁵⁰ Although reported the negative result against *E. coli*, ethanol extracts of aerial parts of *A. paniculata* were found to be effective in inhibiting *E. coli* growth along with other ten gram positive and gram negative bacteria species.⁵¹ The antibacterial activity of three different extracts (dichloromethane, methanol, and aqueous) of *A. paniculata* whole plant was evaluated against 12 skin infection causing pathogenic bacterial strains. methanol extract showed the highest antibacterial activity against *Enterococcus faecalis* at 1000 µg/disc with an inhibition zone of 24mm, and dichloromethane extract showed the least activity against *Neisseria meningitis* at 250 µg/disc with an inhibition zone of 6 mm. and also investigated antibacterial activity of methanol extract of whole plant against five human pathogenic bacteria *S. aureus*, *Streptococcus pyogenes*, *Micrococcus luteus*, *Proteus mirabilis*, and *P. aeruginosa*. Their results revealed that the highest inhibition (19.67 ±0.76 mm) was exerted against *S. aureus* at 1000 µg/mL and the least (07.00 ±1. 50 mm) activity shown against *P. aeruginosae* at 250 µg/mL.⁵²

ANTI INFLAMMATORY ACTIVITY

Andrographis paniculata acts as an anti in flammation drug against histamine, adrenaline, di-methyl benzene etc. Chronic diseases such as cardiovascular disease, cancer and diabetes cause burst release of

inflammatory molecules like macrophage and T lymphocyte production and activation and release of pro inflammatory mediators like tumour necrosis factor (TNF)- α -interleukin (IL)-1, IL-6, interferon (IFN)- γ , nitric oxide (NO) causes inflammation. Effective drug or any inhibitor may reduce the production of these inflammatory molecules which may further reduce inflammation reported that the anti-inflammatory action of dehydroandrographolide was due to its effect on increasing the synthesis and release of adrenocorticotrophic hormone (ACTH) of the pituitary gland of the brain.⁵³⁻⁵⁴ some research also reported that administration of methanolic extract of kalmegh produced complete inhibition of carageenan induced inflammation compared with control models.⁵⁵ The weak anti-inflammatory effects of andrographolide compared to other diterpenoid constituents in the plant, in which the anti-inflammatory effect probably worked by a mechanism that involves secreted material from adrenal glands, since such effects disappeared in adrenalectomized animals.⁵⁶ Oral administration of andrographolide at a dose of 300mg/kg daily had shown significant analgesic activity on acetic-induced writhing in mice and on the Randall-Selitto test in rats, but there was no effect on the hot plate test in mice.⁵⁷ Oral administration of andrographolide at 30,100, and 300mg/kg also showed anti-inflammatory activity in different models in rats.⁵⁸

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CONTRAINDICATION

According to botanical safety handbook this plant falls in class 2b "herb not to be taken during pregnancy".⁵⁹

CONCLUSION

Andrographolide is the major phytoconstituent of *Andrographis paniculata* (Nees) and are potential source of substitute medicines and are widely used to various health diseases. Several researches including in vitro, in vivo (animal), and clinical (human) studies have confirmed various pharmacological activities of plant extracts and products. Andrographolide and its derivatives have anti-inflammatory effects in experimental models asthma, stroke, and arthritis. In recent existence, pharmaceutical chemists have synthesized numerous andrographolide derivatives drug, which show essential pharmacological activities such as those that are anti-inflammatory, antibacterial, antitumor, antidiabetic, anti-HIV, and antiviral. More research is needed to determine the effects of this herb on various metabolizing enzymes and drug interactions for various human diseases

CONFLICT OF INTEREST

Conflict of interest declared none.

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