**A Prospective Review on Phyto-Pharmacological Aspects of Andrographis paniculata**

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**ABSTRACT**

*Andrographis paniculata* Nees is an annual herbaceous plant which belongs to the family Acanthaceae. It is commonly known as Kalmegh, is found in the plains of India, China, Pakistan, Sri Lanka and South Asia and is native to India and Sri Lanka. Kalmegh is known to be the “king of bitters” though it is of small size and it also has a similar appearance and taste as that of the Neem plant. It is one of the widely used effective medicinal plants in the world. All parts of this plant are used to extract the potent phytochemicals, but the composition of phytoconstituents mostly differs from one part to another in a season, place and time of harvest. It is a traditional medicinal plant widely used in the treatment of anti-inflammatory, anti-bacterial, anti-oxidant, hepatoprotective, hematocidal, anti-HIV, anti-cancer, anti-diabetic, arthritis, rheumatism, cough, cold, multiple sclerosis, depression, diarrhoea, dysentery, candida, fevers, herpes, leprosy, malaria, jaundice, tuberculosis and several infectious diseases ranging from malaria to dysentery. The plant is widely used in Ayurvedic and homeopathic system of medicine. The medicinal value of this plant is due to the active ingredients via andrographolide and neoaandrographolide, which are derivative of diterpinoids. It prevents oxidative damage and inhibits binding of toxic metabolite to DNA.

**Key words:** Andrographis paniculata, Anthraceae, Andrographolide, Neoaandrographolide, Kalmegh.

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**INTRODUCTION**

Nature is a rich source of medicinal agents, since the beginning of mankind.1 In Ayurvedic medicine, there are a number of herbs, which have been used traditionally for treating an enormous variety of ailments. Herbal plants are the richest bio-resource on drugs of the ancient system of medicine. Nutraceuticals, modern medicines, folk medicines, pharmaceutical intermediates, chemical entities and also food supplements.2

*Andrographis paniculata*  
*A. paniculata* Nees (Acanthaceae), commonly known as king of bitter, is a perennial herb widely cultivated in India, China, South Asia, South Africa, Pakistan and Sri Lanka. *A. Paniculata* or Kalmegh is one of the enormous herbs used in various Ayurvedic formulations,3 where it is used to treat infections and some diseases, while being used before antibiotics were created. Mostly, the leaves and roots were used for medicinal purpose.

*A. paniculata*, the Kalmega of Ayurveda, is a bristling annual herb eminently bitter in taste in each and every part of the plant body. The plant is known as maha-tita literally “king of bitters” in North Eastern India and known by several vernacular names. It is also known as “Bhui-neem”.

The plant is much smaller in size, exhibits identical appearance and has bitter taste of neem (*Azardirachta indica*). The genus Andrographis consists of 28 species of small annual shrubs basically distributed in tropical Asia. Only a few species are medicinal of which *A. paniculata* is the most popular.4

**Distribution**

*A. paniculata* is distributed in tropical Asian countries frequently in isolated patches. It can be found in various habitative plains, hill slopes, waste lands farms, dry or wetlands, seashore and also road sides. Native population of *A. paniculata* is distributed all over south India and Sri Lanka which may constitute to the origin centre and diversity of species. The herb is also available in northern states of India, Malaysia, Indonesia, West Indies and America. In India, it is probably found in the plains and hilly areas up to 500 m, which accounts for its extensive use. For years, immemorial villages and ethnic communities in India have been using this herb for treating different types of ailments.

**Taxonomic hierarchy**

Kingdom: Plantae  
Division: Angiospermae  
Class: Dicotyledoneae  
Order: Tubiflorae  
Family: Anthraceae  
Genus: Andrographis  
Species: *paniculata* Nees

**Morphology**

*A. paniculata* is an annual, branched, erect plant running ½ to 1 m long in height as shown in the Figure 1. The leaves of *A. paniculata* are dark in color, simple, opposite, lanceolate, glabrous-2 to 12-cm-long, 1- to 3-cm-wide acute apex; entire margin flower consists of small linear 5-particle calyx and tube narrows to about 6-mm-long white corolla with violet marking. Two stamens inserted in the throat and two called as superior pinoids. It prevents oxidative damage and inhibits binding of toxic metabolite to DNA.

**Phytoconstituents**

*A. paniculata* contains diterpenes, lactones and flavonoids. Flavonoids mainly endure in the root and also have been isolated from the leaves. The aerial parts contain alkalines, ketones and aldehydes. Although, it was initially known that the bitter substance in the leaves was the lac-
Andrographolide, a diterpinoid lactone, was isolated from *Andrographis paniculata* (Table 1). The aqueous extract has been reported by Handa and Sharma. The significant chloretic effect of andrographolide is found in conscious rats and anaesthetized guinea pigs. The protection of andrographolide against acetaminophin-induced reaction in volume and contents of bile was better that that produced by silymarin, which was reported by Shukkla et al. Multiple-dose pretreatment with arabinogalactan proteins and andrographolide was protective against ethanol-induced hepatotoxicity in mice and was deemed comparable to the efficacy of silymarin. Kapil and Koul reported that the CCl₄-induced increase in pentobarbitone-induced sleep time in mice is also completely normalized by andrographolide. The intraperitoneal pretreatment for three consecutive days with andrographolide on CCl₄-other butyl hydroperoxide-induced hepatotoxicity in mice was compared with diterpense-andrographiside and neoandrographolide. Both compounds showed a greater protective effect than andrographolide comparable to silymarin and neoandrographolide-normalized glutathione levels.

**Antioxidant activity**

Antioxidant activity and its constituents of *A. paniculata* have been illustrated by various investigators. Oja and Nandava reported that the hydro alcoholic extract of *A. paniculata* prevented isoproterenol-induced evaluated lipid peroxidation and anti-oxidant enzymes activity viz. superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPX) and levels of reduced glutathione level in heart. In addition, the extract also prevented leakage of lactate dehydrogenase (LDH) from the heart and rescued it from isoproterenol-induced myocardial ischaemic injury. The study indicated the anti-oxidant activity of *A. paniculata* and justified its use in heart disease.

Administration of *A. paniculata* prior to diclofenac significantly declines the hepatic anti-oxidant status, i.e., SOD, CAT, GPX, Glutathione S-transferases (GST) and glutathione were increased in the *A. paniculata* plus diclofenac-treated group than in the diclone-treated group. So the result of the Soumendra et al. the study concluded that the aqueous ethanol extract of the *A. paniculata* against diclofenac-induced acute toxicity is mediated either by preventing the refuse of hepatic anti-oxidant status or to its direct radical scavenging capacity. Das et al. reported the nicotin-induced inhibition of mitochondrial electron chain complexes and the resultant increase in nitric oxide (NO) in different parts of rat's brain prevented by simultaneous treatment with the aqueous and ethanol extracts of *A. paniculata*. The aqueous extract exhibited the greater anti-oxidant activity. Andrographolide pretreatment significantly attenuates accumulation of phorbol-12-myristate-13-acetate (PMA)-induced formation of ROS and N-formyl-methionyl-leucyl-aspartate.
phenylalnine (fMLP)-induced adhesion and transmigration of ROS and fMLP-induced adhesion and transmigration of peripheral human neutrophils was only partially reversed by andrographolide. This study suggested that the prevention of ROS production was partly mediated by the direct actuation of protein kinase by PMA and partly mediated by down-regulation of surface MAC-1 expression, an essential integrin for neutrophil adhesion and transmigration, respectively. 

Excessive amounts of NO and prostaglandin E, (PGE) due to expression of inducible isozymes of nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) from activated macrophages play a significant role in inflammatory process. Lipopolysaccharides (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 neandrographolide inhibits LPS-stimulated NO production in a concentration-dependent manner. Andrographolide incubated LPS-induced increase in tumour necrosis factor-alpha (TNF-α) and granulocyte-macrophage colony-stimulating factor. Neoandrographolide also inhibits PGE, synthesis and TNF-α in LPS-stimulated macrophages and its oral administration of mice significantly suppresses dimethylbenzene-induced ear edema acetic acid-induced vascular permeability. 

A. paniculata nees were used for several purposes mainly for treatment of diabetes mellitus. The study evaluated andrographolide for its antiproliferative effect in neonatal streptozotoxin-induced diabetic rats. Andrographolide significantly decreased the levels of blood glucose and improved diabetic rat islet and beta cells. 

Antidiabetic activity

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Anticancer activity

*A. paniculata* is a traditional plant which contributes towards its various biological activities, including anti-cancer property. Hsieh et al. reported that dehydroandrographolide induced autophagy in human oral cancer cells by modulation p53 expression, activating JNK ½ and inhibiting AKT and p38; an administration of dehydroandrographolide effectively suppressed the tumour formation in the oral carcinoma xenograft. 

The first is to study the novel function of dehydroandrographolide in activating autophagy, suggesting that dehydroandrographolide could serve as a new and potential chemopreventive agent for treating human oral cancer. 

The radiosensitizing effect of andrographolide in human ovarian SKOV3 xenograft examined the molecular mechanism of andrographolide-mediated radiosensitization. Nude mice bearing human ovarian SKOV3 were treated with andrographolide to investigate the effect of drug administration to tumour growth, radiosensitivity, apoptosis and autophagy. The result correlated with an increase with Bax/Bcl-2 protein ratio and p-p53 expression after exposure to combination treatment. The level of beclin and Atg5 and the conversion from LC3-I to LC3-II, three important proteins involved in autophagy, were increased. In *in vivo* method, andrographolide acts as a powerful radiosensitizer in human ovarian SKOV3 xenografts and it promotes the Bax/Bcl-2 protein ratio. The activation of caspase-3 leads to enhanced apoptosis as well as autophagy. 

Andrographolide has been reported to have anti-cancer activity in various types of cancer due to its capacity to inactivate the NF-kB pathway. Andrographolide significantly inhibits the proliferation and invasion of Npc cells. The work provides the evidence that the NF-kB pathway is the potential therapeutic target and may also be indispensable in the auto-mediated anti-cancer activities in nasopharyngeal carcinoma.

Top of Form

Zhang et al. reported the protective effect of andrographolide in the development of autoimmune diabetes. Randomly divided four groups of NOD mice were administrated with water and andrographolide at 50, 100 and 150 mg/kg body weight for 4 weeks. Oral glucose tolerance and histopathological insulites were examined. Th1/Th2/Th17 cytokin secretion was determined by ELISA. The transcriptional profits of T-bet, GATA3 and RORyt in the pancreatic lymphatic nude samples derived from the NOD mice were detected by RT-PCR. This protective status correlated with the substantially decreased protection of interferon (IFN)-γ and interleukin (IL)-2 increased IL-10 and transforming growth factor (TGF)-β and α refused IL-17. Andrographolide also increased GATA3 m-RNA expression and decreased T-bet and RORyt m-RNA expressions. The results suggest that andrographolide prevented type I diabetes by maintaining Th1/Th2/Th17 heamostasis. 

Chaursk et al. reported the anti-diabetic potential chlorofluorom fraction of the ethanol effect of *A. paniculata* and diabetes laden gene expression alteration. Streptozotocin (60 mg/kg) induced type two diabetes albino mice. Fasting blood oral glucose tolerance serum liquid profile, tissue glucose in content, glucosys-phosphatase and hexokinase enzymes level in liver in *in vitro* and in *in vivo* insulin estimation were measured on last date of treatment. Biochemical enzymes such as glucose-6- phosphatase and hexokinases were evaluated in body tissues. Apart from this in *in vitro* and in *in vivo* insulin estimation, diabetogenic gene expression analysis of GK, PEPCK, G-6 phase, Gluf-4 AR, PPAR-αy and TNF-α was evaluated using the RT-PCR technique. Anti-diabetic screening of fraction of *A. paniculata* at molecular level revealed significant anti-diabetic activity.

Infectious diseases

Andrographolide is found to be active against pulmonary types of tuberculosis, tuberculosis meningitis and acute pyelonephritis. Intravenous or retrograde intravenous injection of the herb was effective in thrombogritis obliferans especially of "heat toxic type". Ten cases of viper bites were reported to be cured within 3–5 days by a compound which contains *A. paniculata*. A phase I, dose-intense clinical trial of andrographolide was conducted on 13 HIV-positive patients and five HIV-negative healthy volunteers. The administration of andrographolide to HIV-positive patients significantly increased the baseline
mean of CD4+ lymphocyte count from 405 to 501 cells/mm³. There were no significant changes in plasma HIV-1 RNA levels. *A. paniculata* has also been used for uncomplicated upper respiratory tract infections (URTIs).44

CONCLUSION

Andrographolide, main active constituent of *A. paniculata*, is a diterpenoid lactone having a variety of pharmacological effects specified in Ayurveda, Unani, Siddha and Chinese medicine system. This herb has been venerated for treating infectious diseases and highly regarded as having preventative effects against ailments such as liver damage, hyperglycaemia, dysentery, cancer, pulmonary, tuberculosis, AIDS, acute and common cold, flu, myocardial infarction, inflammation and blood clotting. Therefore, further research may be undertaken to develop potent formulations consisting of *A. paniculata* and its isolated molecule, andrographolide, by making use of novel herbal drug delivery system, such as microparticles, vesicular system or through complexation with lipid or other suitable novel carrier.

ABBREVIATIONS

HIF-1: Hypoxia-induced factor-1; HIV: Human immunodeficiency virus; IFN: Interferon; IL: Interleukin; iNOS: isoforms of Nitric Oxide Synthase; JNK: C-Jun N-terminal kinase; LDH: Lactate Dehydrogenase; LPS: Lipopolysaccharides; NO: Nitric oxide; PGE2: Prostaglandin E2; PMA: Phorbol-12-myristate-13-acetate; SOD: Superoxide Dismutase; TNF-α: Tumour Necrosis Factor-alpha; URTIs: Upper respiratory tract infections.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

35. Wang HW, Zhao HY, Xiang SQ. Effects of *Andrographis paniculata* components of nitric acids, endothrin and lipid peroxidation in experimental arthrosclerotic rabbits. Zhongguo Zhong Xi Jie He Za Zhi. 1997;17:547-9. (Article in


