



A REVIEW ON MEDICINAL PROSPECTIVES OF *ANDROGRAPHIS PANICULATA* NEES

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ABSTRACT

Andrographis paniculata Nees (Acanthaceae) is a widely used medicinal plant in China, India, and South Asia. It contains andrographolide as major constituent which impart bitter taste of this herb. Other constituents include 14-deoxy-12-methoxyandrographolide, 14-deoxy-11,12-didehydroandrographolide, 14-deoxyandrographolide. It is used in various ailments like throat infections, dysentery, cancer, hepatotoxicity, cough, cold, headache, edema, pain conditions, inflammation and muscular pain, arthritis, rheumatism, fibro myalgia, multiple sclerosis, depression, diarrhoea, dysentery, cholera, candida, lupus, diabetes, piles, fevers, fatigue, hepatitis, herpes, leprosy, loss of appetite, swollen lymph nodes and other lymphatic conditions, jaundice, malaria, dyspepsia, dermatitis, eczema, burns, pneumonia, bronchitis, tuberculosis, chicken pox, mumps, sluggish liver, spleen, kidneys and adrenal glands, sleeplessness, vaginitis, & constipation. The present review is an attempt to provide recent update on phytochemical and pharmacological profile of *A. paniculata* along with its toxicity and contraindications status.

Keywords: *Andrographis paniculata*, andrographolide, evaluation, medicinal uses.

INTRODUCTION

Andrographis paniculata Nees (Acanthaceae) commonly known as king of bitters, is a perineal herb widely cultivated in China, South Asia, South Africa, India, Pakistan and Sri Lanka. *Andrographis paniculata* or Kalmegh is one of the most widely used herb in various Ayurvedic formulations. The whole plant of *A. paniculata* is used extensively as an anti-inflammatory and antipyretic drug for the treatment of fever, cold, laryngitis, diarrhea, and inflammation. *A. paniculata* was recommended in Charaka Samhita dating back to 175 BC for treatment of jaundice along with other plants in polyherbal preparations. It has also been used traditionally for sluggish liver as an antidote in case of colic dysentery and dyspepsia. It is used as a bitter tonic, antispasmodic, antiperistaltic, stomachic and antihelmintic. It has also been employed with benefit in case of general debility in convalescence after fevers, disorders of liver and advanced stages of dysentery. The juice of fresh leaves, which generally contains andrographolide, is used as a domestic remedy in the treatment of colic pain, loss of appetite, irregular stools and diarrhoea.¹ Since ancient times, *A. paniculata* is known in traditional Asian medicine as an immune system booster, to treat infections in gastrointestinal tract and upper respiratory tract, fever, herpes, sore throat, and a variety of other chronic infectious diseases.² Andrographolide (3 - (2 - (decahydro - 6 - hydroxyl - 5 - (hydroxymethyl) - 5, 8a - dimethyl - 2 - methylenenaphthyl)ethylidene) dihydro - 4 - hydroxyfuran - 2 (3H) - one), neoandrographolide and kalmeghin are the active principles. Besides these active compounds, other chemical constituents include andrograpanoside, andrographanin, 14-deoxy-12-methoxyandrographolide, and deoxyandrographolide.

Taxonomic hierarchy

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

Morphology of leaves of *A. paniculata* : The leaves of *A. paniculata* are dark in color, simple, opposite, lanceolate, glabrous, 2–12cm long, 1–3cm wide; acute apex, entire margin. Flower consists of small, linear 5-particulate Calyx; tube narrows, about 6 mm long white corolla with violet markings. Two stamens, inserted in the throat and two celled superior ovary. 1–2 cm long, 2–5 mm wide, linear-oblong, compressed, erected capsule.³ The photograph of whole plant of *A. paniculata* and its leave can be seen in Plate 1 and Plate 2 respectively.

Microscopy of *A. paniculata*- The leaves of *A. paniculata* have diacytic stomata at leaf's lower epidermis, glandular and non-glandular trichomes, fairly large cystoliths, columnar palisade cells, collenchymas in midrib beneath epidermis; spongy parenchyma cells; vascular bundles of lignified spiral, scalariform and reticulate xylem vessels in the upper part and lignified phloem in the lower part, small acicular calcium oxalate crystals, a layer of wavy-walled lower epidermis cells, dense collenchyma at the corners of stems, a layer of thick-walled endodermis cells and parenchyma contains chloroplastid.³

Chemical Constituents

Therapeutically active constituent of *A. paniculata* / Kalmegh plant is andrographolide which is generally extracted from leaves and aerial parts of *A. paniculata*. It is a colourless diterpene lactone, with bitter taste. Melting point of Andrographolide is 230°-239°C.⁴ (3 - (2 - (Decahydro - 6 - hydroxyl - 5 - (hydroxymethyl) - 5, 8a - dimethyl - 2 - methylenenaphthyl) ethylidene) dihydro - 4 - hydroxyfuran - 2 (3H) - one) is the reported IUPAC name of Andrographolide.

Other reported chemical constituents of *A. paniculata*

Other reported chemical constituents of *A. paniculata* and their uses are given in Table 1 as follows:

It also contains other chemical constituents like 14-deoxy-11,12-didehydroandrographolide, 14-deoxyandrographolide, 3,14-didehydroandrographolide, 14-deoxy-11-oxoandrographolide, neoandrographolide, andrographside and 14-deoxyandrographiside. The structures of some of the principal components are given in figure 1,2,3 and 4.

Pharmacological profile of *A. paniculata*

According to Chinese medicine theory, *A. paniculata* 'cools' and relieves internal heat, inflammation and pain and also used for detoxication.⁵ It is used as bitter tonic, antispasmodic, stomachic and also an antihelmintic. Modern pharmacological studies have demonstrated its hepatoprotective, antithrombotic, anti-inflammatory, immunostimulant, antimalarial, antihyperglycemic and cardioprotective properties.⁶ Research confirmed that if properly administered, *A. paniculata*, has a wide range of pharmacological actions, many of which are very beneficial. The pharmacological update of *A. paniculata* can be covered under the following headings:

Anti-inflammatory

A. paniculata acts as an anti-inflammation 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.⁷ A study demonstrated that intraperitoneal (i.p.) administration of *A. paniculata* methanol extract 50 mg/day for five consecutive days inhibited 65% NO production by peritoneal macrophage and significantly inhibited carageenan induced paw oedema formation in mice. Andrographolide inhibits nitric oxide (NO) production and the expression and stability of inducible synthase (iNOS) protein in lipopolysaccharide (LPS) - stimulated RAW264.7 (RAW) cells.⁵ Andrographolide acts as antioxidant, thereby inhibits the production of neutrophils, macrophage migration, as well as TNF- α and IL-12.

Hepatoprotective

Andrographolide is extensively used as a stimulating agent for liver enzymes and hepatoprotective agent. Andrographolide increases the bile flow and bile salt production. Studies showed that Andrographolide is a potent hepatoprotective agent when compared with silymarin.⁸

Anti-oxidant activity

Hydro alcoholic extract of *A. paniculata* prevented isoproterenol induced elevated lipid per oxidation and antioxidant enzymes activity viz. super oxide dismutase, catalase, glutathione peroxidase and the levels of reduced glutathione level in heart. In addition, the extract also prevented leakage of lactate dehydrogenase from heart and salvaged it from isoproterenol induced myocardial ischemic injury. The study indicated the antioxidant, antilipid peroxidative and antiischemic activity of *A. paniculata* and justified its use in ischemic heart diseases.⁹

Common cold

A randomized double-blinded placebo- controlled clinical trial to study the preventive effect of *A. paniculata* on common cold was conducted on 107 children. They received either andrographis extract tablet or placebo for 3 months during winter season. By the third month, there was found a significant decrease in the incidence of cold in the group taking andrographis compared to those taking placebo. *A. paniculata* prevented and reduced the risk of getting cold by 2.1 times as compared to the placebo.¹⁰

Anti-cancer activity

Methanolic extract of *A. paniculata* was found to have significant toxicity against KB (human epidermoid leukemia)

and P388 (lymphocytic leukemia) cell lines. Bioactivity guided chromatographic fractionation led to the isolation of pure andrographolide from *A. paniculata*, which was proved to be highly toxic to the above-mentioned cell lines. This was the first significant demonstrations of cytotoxic potential of andrographolide. Andrographolide effectively induced cellcycle arrest in cancer cells at G0/G1 stage. Andrographolide also activated the extrinsic death receptor pathway (including caspase-3 and caspase-8) and induced apoptotic cell death in certain human cancer cell types. It has been observed that the alcohol extract of the plant as well as isolated andrographolide were able to induce significant stimulation of both "antigen specific" and "antigen nonspecific" types of immune responses in mice.¹¹

Infectious disease

Andrographolide is found to be active against pulmonary type of tuberculosis, tuberculous meningitis and acute pyelonephritis. Intra-arterial or retrograde intravenous injections of the herb were reported to be effective in thromboangiitis obliterans, especially of "heat toxic type". Ten cases of viper bites were reportedly cured in 3-5 days by a compound formula containing *A. paniculata* as the chief constituent. A phase I, dose-escalating clinical trial of andrographolide was conducted on 13 HIV-positive patients and five HIV-negative healthy volunteers. Andrographolide administration significantly improved the CD4+ lymphocyte count from a baseline mean of 405 cells/mm³ to 501 cells/mm³ in HIV- positive patients. There were no statistically significant changes in mean plasma HIV-1 RNA levels. *A. paniculata* has also been used for uncomplicated upper respiratory tract infections (URTIs).¹²

Anthelmintic activity

The methanol and aqueous extracts of *A. paniculata* were evaluated for its anthelmintic activity against adult earth worms (*Phertima prosthuma*). Three concentrations (25, 50, 75mg/ml) of each extract were studied, which involved the determination of time of paralysis and time of death of the test worms. It was found that both the extracts exhibited significant anthelmintic activity.¹³

Dysentery or Gastroenteritis

Ethanol extract tablets of *A. paniculata* were reported to cure 88.3 percent of acute bacillary dysentery and 91.3 percent of acute gastroenteritis cases. Andrographolide administration was reported to cure 91 percent of acute bacillary dysentery cases.¹²

Anti-hyperglycaemic effects

Ethanol effect of *A. paniculata* increases insulin secretion from the β -cells of islets of langerhens, further mechanism of action of andrographolide is that it enhance the surface uptake of glucose by adipose tissues and inhibit glucose absorption from intestine and glucose production from liver. Oral administration of the ethanol extract of *A. paniculata* effectively reduced the fasting serum glucose level in human.¹⁴

Analgesic and anti-pyretic effects

Oral administration of andrographolide isolated from *A. paniculata* leaves, (30, 100, and 300 mg/kg) was studied for its analgesic and antipyretic effect. Andrographolide did not showed any analgesic activity in hot plate test in mice while it showed significant analgesic activity in acetic acid-induced writhing in mice and Randall Selitto's test in rats at 300 mg/kg dose. Andrographolide (100 and 300 mg/kg) produced significant ($p < 0.05$) anti-pyretic effect after 3 hrs of administration in Brewer's yeast-induced pyrexia in rats.¹⁴

Side effects

Toxicity of andrographolide is not known. As it is called as “King of bitters”, it may cause emesis on over dosing. Gastric instability, loss of appetite and nausea were also observed due to over dosing of andrographolide extract.¹⁰

Contraindications

According to botanical safety handbook, this plant falls in class 2b “herb not to be taken during pregnancy.”¹⁵

CONCLUSION

Andrographolide, main active constituent of *A. paniculata* is a diterpenoid lactone having a variety of pharmacological effects specified in ayurveda, unani, sidhha and traditional chinese medicine system. This herb has been revered for treating infectious diseases and highly regarded as having preventative effects against ailments like liver damage, hyperglycaemia, dysentery, cancer, pulmonary tuberculosis, AIDS, acute and common cold, flu, myocardial infarction, inflammation, blood clotting etc. It has no toxic effects but yet it found unsafe during the pregnancy. Besides a great number of pharmaceutical uses, andrographolide has some side effects like nausea, vomiting, loss of appetite which can only be seen upon overdosing. Therefore, research may further be undertaken to develop potent formulations consisting of *A. paniculata* and its isolated molecule, andrographolide by making use of novel herbal drug delivery systems like microparticles, vesicular systems or through complexation with lipid or other suitable novel carrier.

REFERENCES

- Mishra S, Tiwari SK, Kakkar A, Pandey AK. Chemoprofiling of *Andrographis paniculata* (kalmegh) for its andrographolide content in Madhya Pradesh, India. *Int J Pharm Biol Sci* 2010;1(2):1-5.
- Wangboonskul J, Daodee S, Jarukamjorn K, Sripanidkulchai BO. Pharmacokinetic study of *Andrographis paniculata* tablets in healthy thai male volunteers. *Thai Pharm Health Sci J* 2006;1(3):209-18.
- Bhardwaj A, Khatri P, Soni ML, Ali DJ. Potent herbal hepatoprotective drugs- a review. *J Adv Sci Res* 2011;2(2):15-20.
- Niranjan A, Tiwari SK, Lehri A. Biological activity of kalmegh (*Andrographis paniculata* nees) and its active principle- a review. *Int J Nat Prod Res* 2010;1(2):125-6.
- Chao WW, Lin BF. Isolation and identification of bioactive compounds in *Andrographis paniculata* (*Chuanxinlian*). *Chinese Med* 2010;5(17): 1-15.
- Sule A, Ahmed QU, Samah OA, Omar MN. Bacteriostatic and bactericidal activities of *Andrographis paniculata* extracts on skin disease causing pathogenic bacteria. *J Med Plant Res* 2011;5(1):7-14.

- Sheeja K, Shihab PK, Kuttan G. Antioxidant and anti-inflammatory activities of the plant *Andrographis paniculata* Nees. *Immunopharmacol Immunotoxicol* 2006;28(1):129-40.
- Jarukamjorn K, Nemoto N. Pharmacological aspects of *Andrographis paniculata* on health and its major diterpenoids constituent andrographolide. *J Health Sci* 2008;54(4):370-8.
- Ojha SK, Nandave M, Kumar S, Arya DS. Antioxidant activity of *Andrographis paniculata* in ischemic myocardium of rats. *Global J Pharmacol* 2009;3(3):154-7.
- Denial G. Medicinal uses of *Andrographis*. *International Herb Association*. 2009:8-19.
- Verma A, Padh H, Shrivastava N. Andrographolide: A new plant-derived antineoplastic entity on horizon.
- Akbar S. *Andrographis paniculata*: A review of pharmacological activities and clinical effects. *Int J Health Sci*; author of book Garlic – The Stinking Magic Herb. 16(1):66-77.
- Padma Y, Narasimhudu CL, Devi S, Natha NM. B, Naga R. B, Philip GH. *In vitro* anthelmintic activity of *Andrographis paniculata* (burm.f.) nees. *Int J Pharm Res Develop* 2011;3(3):202-5.
- Rammohan M. Effect of ethanolic extracts of *Andrographis paniculata* on type 2 diabetes mellitus and insulin resistant rats [PhD dissertation]. University Sains Malaysia; 2009 Feb [Cited 2010 Oct 17]. Available on: http://eprints.usm.my/10167/1/effect_of_ethanolic_extracts_of_andrographis_paniculata.pdf
- McGuffin M, Hobbs C, Upton R, Goldberg A.(1997) American Herbal Products Association's Botanical Safety Handbook. CRC Press, Boca Raton, FL. Available on <http://www.amazon.com/American-Products-Associations-Botanical-Handbook>.
- Mohamed Saleem TS. Hepatoprotective herbs – A review. *Int J Res Pharm Sci* 2010;1(1):1-5.
- Kumar AR, Sridevi K, Kumar N V, Nanduri S, Rajagopal S. Anticancer and immunostimulatory compounds from *Andrographis paniculata*. *J Ethnopharmacol* 2004;92(2-3):291-5.
- Lala S, Nandy A K, Mahato S B, Basu M K. Delivery *in-vivo* of 14-deoxy-11-oxoandrographolide, anti-leishmanial agent, by different carriers. *Indian J Biochem Biophys* 2003;40:169-74.
- Liu J, Wang ZT, Ji LL. *In vivo* and *in vitro* anti-inflammatory activities of neoandrographolide. *Am J Chin Med* 2007;35(2):317-28.
- Dahanukar SA, Kulkarni A, Rege NN. Pharmacology of medicinal plants and natural products. *Indian J Pharmacol* 2000;32:81-118.
- Koul IB, Kapil A. Effect of diterpenes from *Andrographis paniculata* on antioxidant defense system and lipid peroxidation. *Indian J Pharmacol* 1994;26:296-300.
- Balachandranm P, Govindarajan R. Cancer—an ayurvedic perspective. *Pharmacol Res* 2005;51:19–30.
- Surveswaran S, Cai YZ, Corke H, Sun M. Systematic evaluation of natural phenolic antioxidants from 133 Indian medicinal plants. *Food Chem* 2007;102(3):938-53

Table 1. Reported chemical constituents of and bioactivities of *A. paniculata*

S. No.	Reported chemical constituent(s)	Pharmacological action(s)	Reference(s)
1.	Andrographolide	Anticancer, hepatoprotective	11,16
2.	14-deoxyandrographolide	Enhanced proliferation and interleukin-2 induction in human peripheral blood lymphocytes	17
3.	14-deoxy-11,12-didehydroandrographolide	Anti-cancer	17
4.	14-deoxy-11-oxoandrographolide	Antileishmaniasis and anti parasitic diseases	18
5.	Neoandrographolide	Anti-inflammatory	19
6.	Andrographide	Liver cleansing and Hepatitis	20
7.	Kalmeghin	Fever and Cold	21
8.	Andrographiside	Anti-oxidant, Anti- Lipoperoxidant, Carcinogenic Detoxification	22,23

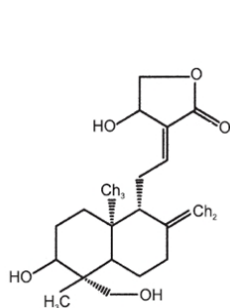


fig 1 -Andrographolide

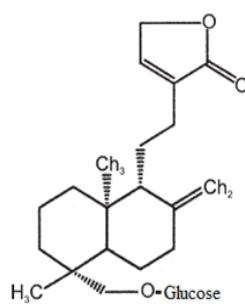


fig 2 -Neoandrographolide

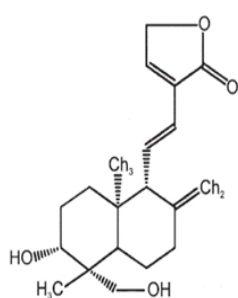


fig 3- 14-Deoxy-11, 12-didehydroandrographolide

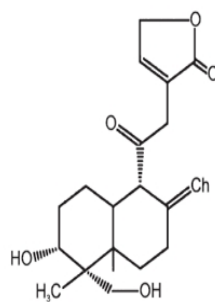


fig 4 -14-Deoxy-11-oxoandrographolide

Plate 1. Whole plant of *A. paniculata*



Plate 2. *A. paniculata* leaves

