

## REVIEW ARTICLE ON THE THERAPEUTIC ACTIVITIES OF *Andrographis Paniculata*

**B. Premkumar\*, K. Sumalatha, C. Nagamani, P. Hari Chander Reddy,  
Mohammed Zahid Hussain, Sudha Vani Kandukuri, Ravi Mishra, Ratna Amancherla**

Bhaskar Pharmacy College, Yenkapally, Moinabad, Hyderabad - 500075, Telangana, India.

### ABSTRACT

*Andrographis paniculata* (Burm.f.) Nees (Acanthaceae) is a medicinal plant traditionally used for the treatment of cold, fever, laryngitis and several infectious diseases ranging from malaria to dysentery and diarrhoea in China, India and other south east Asian countries. It is widely cultivated in Southern and South-eastern Asia, where it is used to treat infections and some diseases, often being used before antibiotics were created. The plant is claimed to possess immunological, anti-bacterial, anti-inflammatory, anti-thrombotic and hepatoprotective properties. The chemical components present in it are Andrographolite, neoandrographolite, and deoxyandrographolide. The derivatives of it are andrographiside, andropanoside, andrographin and panicolin. In this review we shall be going through various aspects of this medicinal plant including its main active constituents, microscopic evaluation and mechanisms of action.

**Keywords:** Chireta, Kalmegh, Anti-bacterial Activity.

### INTRODUCTION

#### *Andrographis Paniculata*:

*A.paniculata* is an herbal medicinal plant native to India, Taiwan, and China. All parts of it have a bitter taste, therefore called as Kalmegh or king of bitters. Benefits of this *A.paniculata* have successfully halted the spread of influenza pandemic in 1919. [1]

Mostly the leaves and roots are used in Indian traditional medicine for treating various ailments, being as bitter tonic, stomachic, flatulence, wounds, ulcers, skin diseases, leprosy, diarrhoea, dysentery, anthelminthic, cardio tonic[2].

#### **Properties of *Andrographis*:**

*Andrographis* has anti-inflammatory, antidiarrheal, antihepatitis, antiviral, antimalarial, hepatoprotective, cardiovascular, anticancer, immunostimulatory properties. It has been used in Siddha and Ayurvedic medicine. In the traditional medicine of India, *A. paniculata* has also been used for jaundice therapy. However male reproductive toxicity and cytotoxicity of the plant have been reported. [3].



**Scientific Classification:**

Kingdom: Plantae

Clade: Tracheophytes

Clade: Angiosperms

Clade: Eudicots

Clade: Asterids

Order: Lamiales

Family: Acanthaceae

Genus: *Andrographis*Species: *A. paniculata*Binomial name: *Andrographis paniculata* (Burm.f.) Nees**Synonyms:**

- *Justicia latebrosa* Russell ex Wall.
- *Justicia paniculata* Burm.f.
- *Justicia stricta* Lam. ex Steud.
- Bhunimba
- Kalamegha
- Kalpanatha
- Tikta
- Yavakaraphala
- Yavatikta [4,5]

**Main Active Constituents**

Andrographolide is the major constituent extracted from the leaves of the plant and is a bicyclic diterpenoid lactone [6]

Its major constituents are:

- Diterpenoids,
- Flavonoids
- Polyphenols [7]

We can obtain the following constituents from the respective parts of the plant:

Leaves: 14-deoxyandrographolide, 14-deoxy-12-hydroxyandrographolide,  $\beta$ -sitosterol, Stigmasterol, Chlorophyll a

Roots: 5, 2'-dihydroxy-7,8-dimethoxyflavone, Long chain trans-cinnamate esters,  $\beta$ -sitosteryl fatty acid esters

Pods: Monogalactosyl diacylglycerols, Lupeol, Triacylglycerols [8].

**Microscopic Evaluation of Leaves:**

The leaf of *A. paniculata* is microphyll, which has an average length of 5.3 cm and width of 1.2 cm. Leaf is dorsiventrally differentiated. The shape of the T.S. of midrib is characteristic, which projects strongly at two corners on the lower side with a prominent ridge having shallow groove in the middle on the adaxial side (Fig.1). Midrib consists of epidemics, collenchyma, mesophyll and vascular tissues (Fig.2a). Collenchymatous hypodermis has 7-8 layers. A collenchyma zone consists of 2-3 layers and is located beneath the hypodermis, which is followed by parenchymatous ground tissues. The midrib possesses an arc of xylem lies in the middle of the ground tissue. Xylem vessels (30-35  $\mu$ m in diameter) arranged in radial rows of 5-6 and phloem lies on abaxial

side. Both the epidermis of the lamina is uniseriate, composed of compactly arranged rectangular cells with cuticle in the outer walls. Cells of the upper epidermis are larger into upper palisade and lower spongy tissues (Fig.2b). A single layer of columnar palisade cells are filled of plenty of chloroplasts. The palisade ratio was found to be about 2. Spongy parenchyma cells are 3 layered, cells of the spongy mesophyll are loosely arranged with wide intercellular spaces. [9]

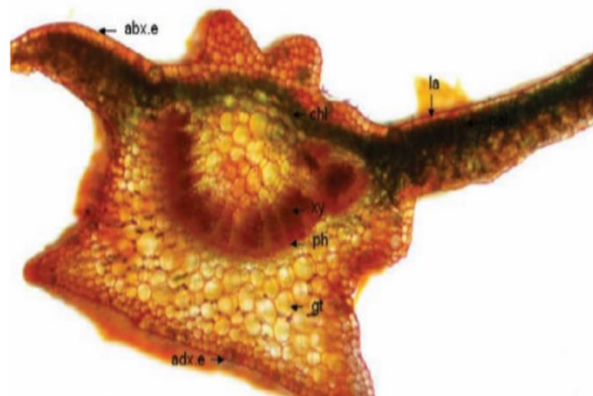


Figure 1. T.S of Lamina with midrib (x4)

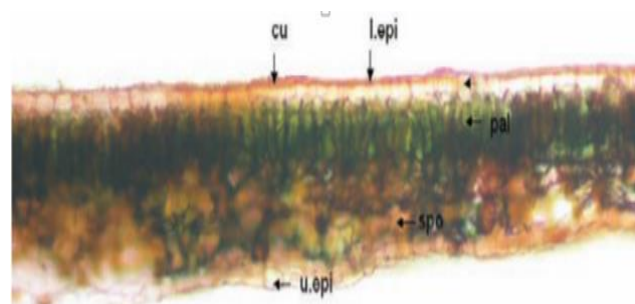


Figure 2a. T.S of Lamina of *Andrographis paniculata* Nees (x10)

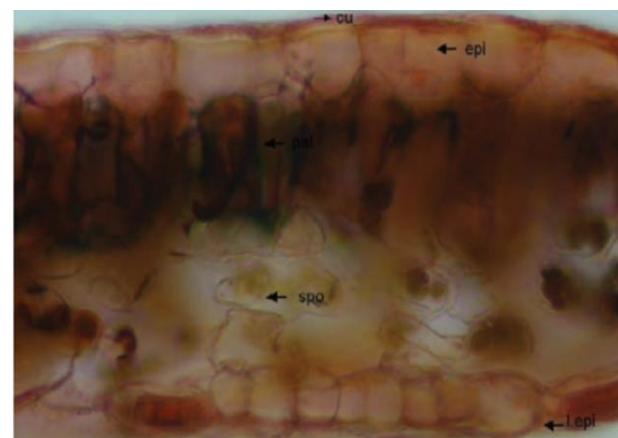
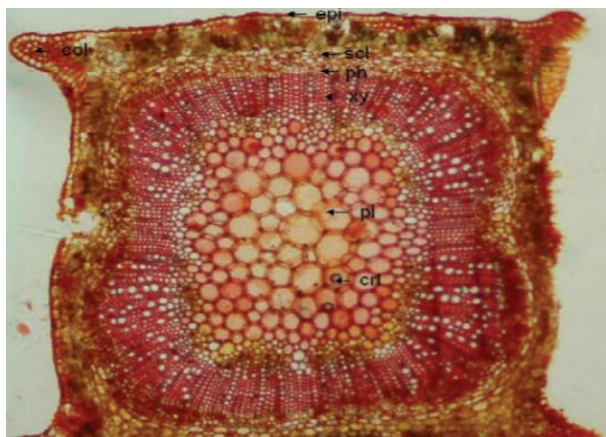


Figure 2. T.S of Lamina of *Andrographis paniculata* Nees (x40)

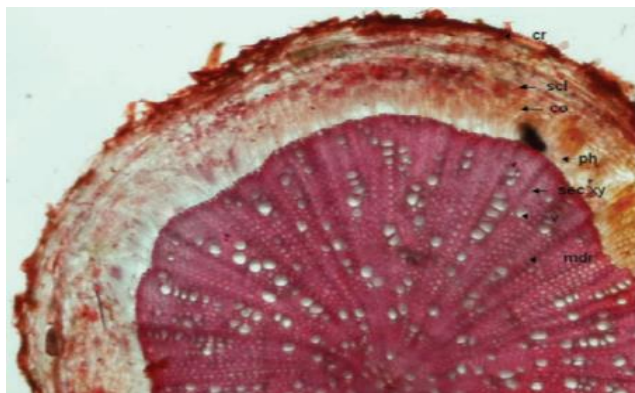
### Microscopic Evaluation of Stem

T.S. of the stem possesses a quadrangular outline with dense collenchyma strands at the four angles of the stem. Epidermis is composed of single layer of rectangular cells. There is a group of 2–3 layered collenchymas cell zone with secretory cavities having white colored deposition are present under the epidermis. Cortex forms a narrow zone, composed of 5–6 layers of parenchyma cells with chloroplast. Solitary sclereids and a group of sclereids of 4–6 are present in the cortex followed by a layer of thick-walled endodermis and parenchyma contains chloroplast. Solitary sclereids are present in secondary phloem tissues. Xylem is very prominent and occupies the major portion of the stem. Vessels are mostly solitary and small sized majority of them are arranged in radial rows. Vessels are circular or polygonal in shape.



### Microscopic Evaluation of Root

Conspicuous cork is composed of 8–10 layers. Outer 2–3 layers are thick walled cells filled with brown content, followed by 6–7 layers of thin walled ranges from 7.4–11.6  $\mu\text{m}$  and 24.7–42.2  $\mu\text{m}$  in length. Radial longitudinal section showed the vessel to vessel pitting was in alternate position. The pits moderately sparse and pit aperture about 2.69  $\mu\text{m}$  in diameter.



### Powder Microscopy

The dried leaves, root and stem of *A.paniculata* were analysed for powder characteristics. Microscopical examination showed fragments of leaf epidermis with diacytic, stomata and fairly large cystoliths in upper and lower epidermis. Stem and root powder showed abundant pyramidal calcium oxalate crystals. Vessel elements with bordered pits and intervessel pitting in alternate position and lignified fibres with pointed ends were observed. Fragment of parenchymatous tissues of cortex were also observed.

### Mechanisms of Action

#### Anti-bacterial Activity

To evaluate the anti-microbial activity of *A.paniculata* extracts, nine species (strains of microorganisms were selected, *Klebsiella pneumonia*, *Bacillus subtilis*, *Aeromonas hydrophilia*, *Proteus vulgaris*, *Salmonella typhi*, *Staphylococcus aureus*, *Streptococcus pyogens*, *Escherichia coli* were collected and sub cultured in nutrient agar medium, and used for anti-microbial susceptibility test. (10) In the present investigation chloroform and methanol extracts obtained from *A.paniculata* were studied against *K.pneumonia*, *B.subtilis*, *A.hydrophilia*, *P.vulgaris*, *S.typhi*, *S.aureus*, *S.pyrogens*, *E.coli* and *P.aeruginosa* using agar well diffusion method.(11) Effective bacterial activity was observed in middle (150mg) and higher doses (200mg) of chloroform and all the doses of methanol extracts of *A.paniculata* against *Klebsiella pneumonia* and *Bacillus subtilis* with the zone of inhibition ranging from 10–16mm, The higher dose (200mg) of methanol extract inhibited the growth of *Aeromonas hydrophilia* and *Proteus vulgaris* (zone of inhibition 12mm), the growth of *Salmonella typhi* was inhibited by mid(150mg) and higher dose (200mg) of methanol extract (zone of inhibition 12mm). all the doses of chloroform extract potentially inhibited the growth of staphylococcus aureus with zone of inhibition ranging from 10–16mm. the higher dose (200mg) of chloroform extract inhibited the growth of *Streptococcus pyrogens* (zone of inhibition 11mm). The growth *E.coli* was inhibited by mid (150mg) and higher dose (200mg) of chloroform and methanol extract of *A.paniculata* with zone of inhibition ranging from 10–13mm. None of the extracts inhibited the growth of *Pseudomonas aeruginosa*. Examination reveals that chloroform and methanol extracts of *A.paniculata* act as significant growth inhibition against pathogens and act as a potent anti-microbial activator.

#### Hepatoprotective activity

*Andrographis paniculata* (Kalmegh) is used as a hepatoprotective and hepatostimulative agent and is highly recommended in the Indian traditional system of medicine. The aqueous extract of the leaves of this plant

has traditionally been used for treatment of various liver disorders and jaundice. Around twenty six different remedies including *Andrographis paniculata* have been used to treat liver disorders in traditional Ayurveda medicine. Andrographolide, which is the main constituent of *Andrographis paniculata*, was found to be effective in preventing carbon tetrachloride induced liver damage (Rats and mice). Andrographolide also showed remarkable hepatoprotective activity against different types of liver damage which induced by paracetamol or galactosamine, and had a higher capacity than a classical antioxidant Silymarin in preventing the decrease of bile production induced by paracetamol. [12] Andrographolide was suggested to play an effective role as potent stimulator of gall bladder function by producing a significant increase in bile flow, bile salts and bile acid in conscious rats and anesthetized guinea pigs. There was distinct improvement in the majority of infective hepatitis patients after continuous treatment with *Andrographis paniculata*, i.e., improvement of appetite and liver function tests, regular recovery from jaundice, and subsidence of fever [13].

#### Anti-diabetic activity

Andrographolide and 14-deoxy-11,12-didehydroandrographolide isolated from the alcoholic extract of the aerial parts of *A. paniculata* reduced the phenotypes indicating diabetic nephropathy in MES-13 cells, which include secretion of extracellular matrix protein fibronectin, cytokine TGF- $\beta$ , states of oxidative stress, and apoptosis marker caspase-3. Compound 14-deoxy-11,12-didehydroandrographolide showed more potent activity than andrographolide in the reduction of apoptosis marker caspase-3, fibrosis marker cytokine TGF- $\beta$ , and plasminogen activator inhibitor-1. Both compounds also reduced reactive oxygen species in the MES-13 cells [14].

The aqueous extract (50 mg/kg) of *A. paniculata* raw material produced a significant ( $P < 0.05$ ) reduction (52.9%) in blood glucose level in streptozocin-induced hyperglycaemic rats. Freeze dried material of *A. paniculata* (6.25 mg/kg body weight), however, produced a more significant ( $P < 0.001$ ) reduction (61.81%) in blood glucose level. The results further showed that the aqueous extract of *A. paniculata* did not produce significant reduction in blood glucose level in normoglycemic rats.

#### Immunological potential

Some recent research had indicated that extract of *Andrographis paniculata*, may have the potential for interfering with the viability of the human immune-deficiency virus (HIV) and advised that *A. paniculata*, could combine with modern medicines against acquired immunodeficiency syndrome (AIDS). Andrographolide, which is the important constituent of

*A. paniculata*, can interrupt or modify the cellular signal transduction pathway of the virus, consequently interfering with the key enzymes and viral reproduction [15]. *Andrographis paniculata*, was proposed as a potent stimulator of the immune system by two approaches. First was as an antigen specific response; in which the antibodies were made to counteract invading microbes and the second was as a nonspecific immune response; macrophage cells scavenged and destroyed invaders. Since *A. paniculata* activated both responses, it may be effective against a variety of infectious and oncogenic agents.

#### Anti-inflammatory activity

In the experiment involving Carrageenan-induced pedal oedema in rats, the rats were injected with 0.1 ml of a 1% carrageenan solution in saline into the sub-plantar region of the left hind paw 60 min after 10th consecutive daily drug treatments, the diabetic rats showed significant ( $p < 0.05$ ) increased pedal oedema volume compared to non-diabetic control rats on day 10. However, diabetic rats treated with 10 repeated daily dose of AP (100, 200 and 400 mg/kg), or andrographolide (30, 60 and 120 mg/kg) demonstrated significant ( $p < 0.05$ ) decreased pedal oedema volume (Figure 4A). Qualitatively, the efficacies of AP and andrographolide were similar to standard drug indomethacin, thus proving the anti-inflammatory activity of *Andrographis paniculata* [16]. Therefore, due to its excellent anti-inflammatory activity, andrographolide has been evaluated for its anti-angiogenic potential as well as an anti-angiogenic prospects. Andrographolide could successfully inhibit the tumor specific capillary sprouting without damaging the pre-existing vasculature. *in vitro* as well as *in vivo* andrographolide also down regulated the production of various angiogenic factors like vascular endothelial growth factor (VEGF), Nitric Oxide (NO) and pro-inflammatory cytokines and grand the levels of anti-angiogenic factors like IL-2 and tissue inhibitor of (TIMP-1) metalloproteinase [17].

#### Anti-fertility and pregnancy terminating effect

*Andrographis paniculata*, found to obsessed anti-fertility and pregnancy-terminating effects and stopped spermatogenesis in male rats. No one female mouse that daily consumed *Andrographis paniculata*, mixed food became pregnant when mated with the male of potential fertility who did not receive the treatment. The observations suggested an anti-spermatogenic or anti-androgenic abilities as well as ovulation preventive effect of the plant. Hence using of the herb during pregnancy should be avoided. The study pointed to a male reproductive toxic effect of a therapeutic use of andrographolide and confirmed the possible prospective use of andrographolide as a male contraceptive. Changes

in the biochemical parameters in rats, such as significant decreases in protein content, but marked increases in cholesterol, acid phosphatase, and alkaline phosphatase levels with appearance of fructose in the reproductive system, recommended anti-fertility effects of the andrographolide [18].

### Toxicity

The safety of *A. paniculata* extract in genotoxic tests has been reported and also the LD50 value has been determined to be more than 5 g/kg rat body weight in an oral acute toxicity study [19]. Testicular toxicity as assessed by reproductive organ weight, testicular histology, ultra structural analysis of Leydig cells and testosterone levels was not found after 60 d treatment of Sprague Dawley rats with ethanol extract of the dried herbs of *A. paniculata* at doses of 20, 200 and 1 000 mg/kg suggesting the relative safe toxicity profile. [20]

### REFERENCES

1. Anonymous. <https://pubmed.ncbi.nlm.nih.gov/30444296/>
2. Akbar S. Andrographis paniculata: a review of pharmacological activities and clinical effects,” *Alternative Medicine Review*, vol. 16, no. 1, pp. 66–77, 2011.
3. Akbarsha, M.A., Murugaian, P. Aspects of the male reproductive toxicity/male antifertility property of andrographolide in albino rats: Effect on the testis and the cauda epididymidal spermatozoa. *Phytother Res.* 2000. 14;432-435.
4. <https://plants.usda.gov/java/ClassificationServlet?source=profile&symbol=ANPA2&display=31>
5. <https://ayushvedah.com/druginfo.php?drugid=101&info=synon>
6. Yan Dai, Shao-Ru Chen, Ling Chai, Jing Zhao, Yitao Wang & Ying Wang (2019). "Overview of pharmacological activities of Andrographis paniculata and its major compound andrographolide". *Critical Reviews in Food Science and Nutrition*. 59 (sup1): S17–S29.
7. Chao W-W, Lin B-F. Isolation and identification of bioactive compounds in Andrographis paniculata (Chuanxinlian). *Chin Med* 2010; 5:17.
8. <http://impactfactor.org/PDF/IJPPR/8/IJPPR,Vol8,Issue8,Article21.pdf>
9. Botanical pharmacognosy of Andrographis paniculata (Burm. F.) Wall. Ex. Nees Sudhakaran MV
10. Murry PR, Baron EJ, Pfaller MA, Tenover FC, Yolken HR. *Manual of clinical microbiology*, 6th edition, ASM press, Washington, Dc 1995, 15-18.
11. Geetha I, Catherine P, Alexander S, Antibacterial activity of Andrographis paniculata extracts 2017;6(5):01-04.
12. Handa, S.S., Sharma, A. Hepatoprotective activity of andrographolide from Andrographis paniculata, against carbontetrachloride. *Indian J. Med. Res.*, 1990. 92: 276-283.
13. Shukla, B., Visen, P.K.S. and Dhawan, B.N. Choloretic effect of andrographolide in rats and guinea pigs. *Planta Med.* 1992. 58: 146-148.
14. Lee MJ, Rao YK, Chen K, Lee YC, Chung YS, Teng YM. Andrographolide and 14-deoxy-11,12-didehydroandrographolide from Andrographis paniculata attenuates high glucose-induced fibrosis and apoptosis in murine renal mesangial cell lines. *J Ethnopharmacol.* 2010;132:497–505.
15. Stephen, H. and Comac, L. *Miracle herbs: how herbs combine with modern medicine to treat cancer, heart disease, AIDS, and more.* Kensington Publishing Corporation; 2000.
16. <https://www.echronicon.com/ecps/pharmaceutical-science-ECPS-01-00004.php>
17. Zhao, F., He, E.Q., Wang, L., Liu, K. Anti-tumor activities of andrographolide, a diterpene from Andrographis paniculata, by inducing apoptosis and inhibiting VEGF level. *J. Asian Nat. Prod. Res.*, 2008. 10: 473–479.
18. Janarthanan, S. Antifertility effects of andrographolide in rats. *J. Ecobio.*, 1990. 2: 325-329.
19. Chandrasekaran CV, Thiagarajan P, Sundarajan K, Goudar KS, Deepak M, Murali B, et al. Evaluation of the genotoxic potential and acute oral toxicity of standardized extract of Andrographis paniculata (Kalmcold) *Food Chem Toxicol.* 2009;47:1892–1902.

### CONCLUSION

Medicinal plants are economically very essential, as they contain active constituents that are used in the treatment of many human diseases. From the above review, it is clear that *Andrographis paniculata* shows a wide range of therapeutic activities such as the plant is considered a potential source of antibacterial agent to develop new antibiotics, so there is an urgent need to isolate novel compounds from it so as to make a healthy tomorrow with its highly applied therapeutic agents for a variety of disorders in the near future to cure human diseases as well as some animal diseases. To fulfil this dream, the researchers might focus on multiplication of this plant to meet commercial demand besides the pharmacology study. Tissue culture techniques might be a good alternative to make *A. paniculata* available for researches (i.e., pharmacological study and phytochemical study to find new bioactive compounds) as well as conservation of this plant.

20. Burgos RA, Caballero EE, Sanchez NS, Schroeder RA, Wikman GK, Hancke JL. Testicular toxicity assessment of *Andrographis paniculata* dried extract in rats. *J Ethnopharmacol.* 1997;58:219–224.



This work is licensed under a Creative Commons Attribution-NonCommercial 3.0 Unported License.