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REVIEW ARTICLE

Andrographis paniculata: a review of pharmacology and clinical efficacy

Sangita Boro[1], Manisha Chirania[1], Deepjyoti Boro[1], Bhriganka Bharadwaj[1] Mitali Baruah[2], and Minakshi Bhattacharjee[2]*

[1]Programme of Microbiology, Assam down town University, Panikhaiti, Guwahati- 781026, Assam, India

[2]Programme of Biotechnology, Assam down town University, Panikhaiti, Guwahati- 781026, Assam. India

*** Correspondence Author:**

minakshi.bhattacharjee@adtu.in

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ABSTRACT

Andrographis paniculata is widely regarded as one of the most important medicinal plants due to its broad therapeutic value and global use in traditional medicine. Commonly known as *Kalmegh*, *creat*, or green *chirayata*, the plant has been an integral part of Ayurvedic, Siddha, Unani, and other traditional healing systems for centuries. It has traditionally been consumed to manage a variety of ailments, particularly those related to the liver, respiratory system, and immune health. Phytochemical investigations have revealed that *Andrographis paniculata* is rich in diverse bioactive constituents. Among these, andrographolide, neoandrographolide, and didehydroandrographolide are the most prominent diterpenoid lactones. Andrographolide, in particular, is recognized as the principal active compound and has been extensively studied for its wide pharmacological spectrum. Research indicates that andrographolide exhibits strong hepatoprotective, antioxidant, anti-inflammatory, immunomodulatory, antibacterial, antipyretic, anti-diabetic, and anti-cancer activities. These properties contribute to the plant's reputation as a versatile therapeutic agent. In this review, we systematically searched and analyzed articles published in English from 2019 to 2025, using PubMed, ScienceDirect, Springer Link, and Google Scholar. Relevant search terms included "*Andrographis paniculata*", pharmacology", "clinical efficacy", "safety", etc. Given its chemical richness and diverse pharmacological actions, *Andrographis paniculata* continues to attract scientific attention. Numerous studies support its potential in managing chronic diseases, enhancing immune function, and mitigating oxidative stress. This review aims to provide a concise yet comprehensive overview of the plant's therapeutic relevance, highlighting its major chemical constituents and summarizing key findings from pharmacological evaluations and clinical safety and efficacy reported in the scientific literature. By synthesizing existing knowledge, this review emphasises the significance of *Andrographis paniculata* as a promising natural resource in herbal medicine and modern pharmacotherapy.

Keywords: Kalmegh, *Andrographis paniculata*, medicinal plant, andrographolide.

Abbreviations :
CCWHS : common cold with wind-heat syndrome
CRC : colorectal cancer
CYP450: cytochrome P450

DES : deep eutectic solvents
DKK1 :Dickkopf-related protein 1
fMLP N : formyl-methionyl-leucyl-phenylalanine
HCoV-OC43 : human corona virus
HIF-1α : hypoxia-inducible factor 1-alpha
HIV : human immunodeficiency virus
HPV : human papilloma virus
H3N2: hemagglutinin type 3 and neuraminidase type 2
IGF-IR : insulin-like growth factor-I
MAPK1 : mitogen-activated protein kinase 1
NF-κB : Nuclear factor kappa-light-chain-enhancer of activated B cells
PI3K/Akt : phosphatidylinositol 3-kinase/ protein kinase B
PPAP- α : polycyclic polyprenylated acylphloroglucinol
SPLA2 : secretory phospholipase A2
STAT3 : signal transducer and activator of transcription 3
TXB2 : thromboxane B2
URIs : upper respiratory infections
VEGF : vascular endothelial growth factor

INTRODUCTION

Andrographis paniculata is an excellent beneficial plant due to its wide therapeutic value and long-standing use in traditional medicine. Traditionally, it is known as *Kalmegh*, *creat*, or green *chirayata*. It has been documented as being used in various systems of alternative medicine such as Ayurvedic, Siddha, and Unani for centuries. *Andrographis paniculata* is widely recognized as "King of Bitters," because of its extremely bitter taste. In addition, it is called *Bhui Neem*," or "ground neem." It is a herbaceous plant that is indigenous to Sri Lanka and India and belongs the *Acanthaceae* family.[1] Historically, it has long served as a remedy for various illnesses. Structurally, the plant is an erect herb that grows to a height of 30 to 110 cm. The leaves are lanceolate, measuring up to 8 cm (3.1 in) long by 2.5 cm wide (0.98 in). Pink single flowers are placed in loosely spreading racemes or panicles. The fruits are capsule shaped, about 2 cm (0.79 in) long, and having many yellowish-brown seeds.[2] The flowering period ranges from September to December.[3]

Modern science is focusing on validating the traditional claims of this plant through systemic investigations. Different extracts (i.e. acetone, chloroform, ethanol, hexane, methanolic or aqueous extract) and isolated pure metabolites from *A. paniculata* have been investigated for pharmacological properties, for example, antibacterial, antiviral, antifungal, antiparasitic, choleretic, hypocholesterolemic, anti-inflammatory, anti-hyperglycemic, hepatoprotective, anticancer, immunomodulatory, cardiovascular, antihyperlipidemic, emollient, anti-snake venom, anti-platelet aggregation, anti-fertility, carminative, and antipyretic properties at in vitro and in vivo conditions.[4-6] Recently, scientists discovered novel pharmacological functions, working mechanisms, and structure-activity relationships in *Andrographis paniculata*. This review highlights the medicinal aspects of *Andrographis paniculata* which exhibits a wide range of therapeutic activities, including anti-inflammatory, hepatoprotective, antioxidant, immunostimulatory, antimicrobial, anticancer, and metabolic benefits. The major bioactive component is andrographolide, which plays a pivotal role in the aforelisted benefits, hence making this plant very lucrative for drug development. All these aspects have been discussed categorically.

METHODS

In this review, we searched the literature for articles on *Andrographis paniculata* published in English between 2019 and 2025. Relevant articles were retrieved from PubMed, ScienceDirect, SpringerLink, and Google Scholar using the key words "*Andrographis paniculata*", "pharmacology," "acute respiratory tract infections", "antimicrobial agents", "invasive microbes," and "medicinal". The search initially yielded 184 articles. After removing duplicates, inaccessible full texts, and articles not relevant to

the review objectives, 65 articles were excluded. For searching the controlled clinical trials, the following keywords "antiparasitic", "clinical trials", "controlled clinical trials", and "randomized clinical trials" were used in PubMed, Scopus, and Web of Science. Controlled clinical trials were systematically screened and selected for further evaluation of their outcomes in this study. A total of 95 articles were selected for analysis and synthesis (as shown in Figure 1).

Andrographis paniculata (Figure 2) leaves and roots have been traditionally utilized since times immemorial in Asia and European countries to cure a wide range of health problems. However, the entire plant is also employed for a few specific uses. In Indian medical systems, it is regarded as a hepatoprotective agent. It is used in skin infections (topically), diabetes, diarrhea, enteritis, helminthiasis, herpes, peptic ulcers, and snake bites (topically).[5] In the Unani medicinal system, it is employed as a carminative, anthelmintic, emollient, astringent, diuretic, emmenagogue, stomach and liver tonic, and antipyretic. It is recommended for the treatment of boils and skin eruptions, leprosy, gonorrhoea, scabies, and chronic and seasonal fevers due to its "blood purifying" characteristics. To treat fussiness, constipation, and appetite loss in newborns, fresh leaf infusion is administered.[6] In China, the herb is considered to have anti-viral, antipyretic, anti-inflammatory and anti-venom properties. Various formulations and chemical preparations of *A. paniculata* are used for treating pharyngo-laryngitis, pneumonia, respiratory tract infections, otitis, tonsillitis, vaginitis, dysentery, eczema, epidemic encephalitis B, hepatitis, herpes zoster, laryngitis, mumps, neonatal subcutaneous annular ulcer, neurodermatitis, etc.[6-8] In traditional Bangladesh, it is used as a hepato-protectant, anti-diabetic, anti-microbial, anti-inflammatory, and anti-malarial.[9]

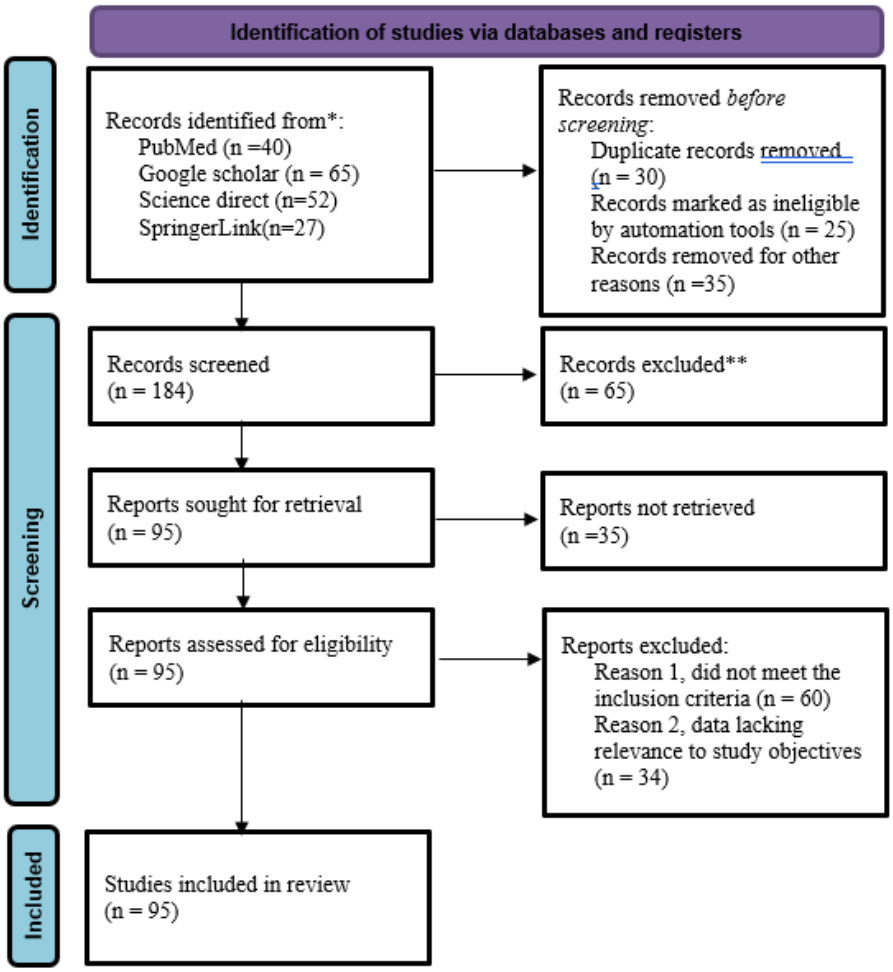

Figure 1. Identification of studies via databases and registers

Figure 2. *Andrographis paniculata* plant

Pharmacological activity of andrographolide
Hepatoprotective effects of A. paniculata extract

Osemwenkhae et al.[9] reported that significant increases in serum levels of marker enzymes [alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP)] and bilirubin [total bilirubin (TBL) and direct bilirubin (DBL)] and a decrease in total protein (TP), albumin (ALB), high-density lipoprotein (HDL) cholesterol and reduced glutathione (GSH) in CCl4 intoxicated rats returned to normal when treated with *A. paniculata* extract, indicating that it has hepatoprotective properties.[9] Ren et al.[10] reported that pre-treatment of mice with induced hepatotoxicity with the diterpenes andrographolide, andrographiside, and neoandrographolide isolated from *Andrographis paniculata,* resulted in a considerable decrease in the production of malondialdehyde, depletion of reduced glutathione (GSH), and decreased glutamic-pyruvate transaminase (GPT) enzymatic leakage and alkaline phosphatase (AP). Andrographolide exhibited lower efficiency than did andrographiside and neoandrographolide which were as effective as silymarin, indicating that andrographolide is not the only substance responsible for the hepatoprotective action.

Trivedi et al. [11] observed that raw extract of *A. paniculata* and andrographolide was protective against hexachlorocyclohexane in mice and in turn resulted in higher activity of hepatic glutathione, glutathione reductase (GR), glutathione peroxidase (GSH-Px), superoxide dismutase (SOD), and catalase (CAT). The activity of γ-glutamyl transpeptidase (γ-GTP) and glutathione-S-transferase (GST) was reduced. The extract was also protective against galactosamine-induced liver defects in rats and prevented changes in biochemical parameters and liver histology. A similar effect was shown in rats given andrographolide after an acetaminophen challenge, and also in an ex vivo preparation of isolated rat hepatocytes.[12, 13]

Suriyo et al.[14] reported that *A. paniculata* crude extract and andrographolide suppressed hepatic cytochrome P450 (CYP) activities in human liver microsomes.

Anti-inflammatory activities of *A. paniculata* methanolic extract

Systemic inflammation is associated with a greater chance of developing long term illnesses, such as cancer, diabetes, and heart disease. *A. paniculata* is reported to have antioxidant and anti-inflammatory properties by several researchers. Ardika et al.[15] reported that *A. paniculata* significantly decreased the activity of NF-κB luciferase, tumor necrosis factor (TNF), interleukin 6 (IL-6), macrophage inflammatory protein-2 (MIP-2), nitric oxide (NO) secretions from LPS/interferon-stimulated Raw 264.7 cells, and inflammatory cell infiltration into the mouse lung. MIP-2 mRNA expression in the brain was also shown to have significantly decreased.

Albornoz et al.[16] observed that andrographolide reduces nitric oxide production by inhibiting iNOS gene expression in vitro. Furthermore, andrographolide significantly decreased the activity of NF-κB by forming a covalent adduct with the reduced cysteine 62 of p50, which prevented the binding of NF-κB oligonucleotides to nuclear proteins.[17] Mehta et al. [18] found that compounds from *A. paniculata*, including andrographolide, isoandrographolide 7-O-methylwogonin, and skullcapflavone-I, significantly reduced the generation of NO and PGE2 in J774A.1 macrophages. The LPS-stimulated NO production was decreased when *A. paniculata* methanol extract was added to BCG-induced macrophages. The bioactive compounds in the plant extract were the diterpene lactones andrographolide and neoandrographolide.[18]

Antioxidant activities of *A. paniculata* extract

Ali et al.[19] reported that administration of *A. paniculata* demonstrated protective effects on the levels and activities of superoxide dismutase, catalase, glutathione peroxidase, and glutathione. Lipid peroxidase activity was also reduced. Research by Zarezadeh et al.[20] highlights the significant potential of specific natural compounds to interact with and regulate signal transducer and activator of transcription 3 (STAT3) molecules. As a transcription factor, STAT3 plays a fundamental role in maintaining cell viability and driving growth. However, when overactive, it becomes a major driver of malignancy by accelerating the proliferation and spread of cancer cells, helping tumors evade the immune system, and promoting cell survival mechanisms that resist treatment. Because of these effects, the scientific community is increasingly focusing on identifying natural inhibitors that can disrupt STAT3 signaling. Targeting this pathway is currently considered a high-priority strategy for developing the next generation of non-toxic, effective cancer therapies.[20] A study by Lu [21] et al. says that pre-treatment with andrographolide was observed to dramatically inhibit the adherence of rat neutrophils produced by N-formyl-methionyl-leucyl-phenylalanine (fMLP), lower the accumulation of phorbol-12-myristate-13-acetate (PMA), and ROS. Singh et al.[22] also observed that medicinal plants and their biotic compounds can inhibit foam cell formation (which leads to atherosclerotic lesions) by targeting the regulatory factors such as suppressing cholesterol transporter, inhibiting ACAT and neutral cholesteryl ester hydrolase activities. *A. paniculata* supplementation lowers nicotine-induced toxicity in lymphocytes by lowering superoxide-mediated oxidative stress, lipid peroxidation, protein oxidation, and DNA fragmentation, and by increasing cell viability as well as the activities of antioxidant enzymes, superoxide dismutase (SOD), and reduced glutathione (GSH).[23] The extract of *A. paniculata* dramatically reduced malondialdehyde (MDA) levels and increased total antioxidant status in rat urine samples collected 24 hours after oral administration.[24]

Antidiabetic and anti-hyperlipidemic effects of *A. paniculata* extract

Sasongko et al.[25] reported that combination therapy including catfish oil with *Andrographis paniculata* possesses antihyperglycemic and lipid-modulating effect. Oral application of the plant extract reduced the elevated glucose parameters in streptozotocin-diabetic rats which resembled that of metformin-treated groups. The extract significantly reduced hepatic glucose-6-phosphatase (G-6-Pase) activity and lowered fasting blood triglyceride levels by 49.8 percent, compared to 27.7 percent with metformin. [26] Ogunlana et al. [27] demonstrated that twig extract of the plant *Andrographis paniculata* significantly lowers fasting blood glucose level and increases glucose tolerance in STZ-induced diabetic rats, with its activity showing superiority to metformin. Rehman et al.[28] reported that *A. paniculata* possesses therapeutic potential due to its phytochemical constituents such as diterpenoids and flavonoids. Emmanuel et al.[29] demonstrated that powdered leaves of *A. paniculata* when provided along with the diet has the potential to reverse or reduce obesity linked metabolic disorders in Wistar rats. Hidayat et al.[30] reported that therapy with *A. paniculata* extract at doses of 200-400 mg/kg improved the kidney hypertrophy index in STZ-diabetic rats. In addition to this, superoxide dismutase (SOD), catalase, and glutathione (GSH) activities in the kidney of STZ-diabetic rats increased after the administration. Chatterjee et al.[31] showed that *A. paniculata* has antihyperglycemic as well as neuroprotective effect and is used to reduce diabetes related mental health problems.

Anti-pyretic effect of *A. paniculata* extract

Ilmi et al.[32] reported that at a dose of 100mg/g body weight (BW), administration of *A. paniculata* ethyl acetate fraction to male rats with yeast-induced pyrexia, resulted in a substantial antipyretic effect as compared to the negative control groups. Mundada et al.[33] also reported that *A. paniculata* has antimicrobial, anti-inflammatory, and organ-protective activities. Suebsasana et al.[34] showed that andrographolide and 14-deoxy-11,12-didehydroandrographolide derived from *A. paniculata* showed potential analgesic, antipyretic and anti-inflammatory activity with no serious side effects. Pokala et al.[35] showed that leaf extract of *A. paniculata* had antipyretic activity in febrile rabbits exhibiting delayed but sustained effects.

***A. paniculata* extracts as antimicrobial and antiparasitic agents**

Parmar et al.[36] noted that the methanolic and ethanolic extracts of *A.paniculata* had greater

antimicrobial effect than the petroleum ether extract. Hossain et al.[8] found that andrographolide, derived from *A. paniculata*, can inhibit virulence factors in invasive microbes and regulate host immunity. Dafur et al. [37] demonstrated that andrographolide, which is an important bio-active compound derived from *A.paniculata* showed a wide range of anti-microbial as well as anti-protozoal effects against a large number of pathogens. Das and Srivastav [38] showed that the methanolic extract of the plant had significant anti-microbial effects against *E. coli and B. subtilis* owing to its phytochemical constituents. Yarnvitayalert et al. [39] demonstrated that andrographolide also shows anti-viral activity. Prasetyo et al.[40] revealed that *A. paniculata* increased TGF expression, reduced TLR-4 expression, and raised the apoptosis index of placental tissue in pregnant mice infected with *Plasmodium berghei,* by suppressing Cox-2 and prostaglandin expression, and thus, avoided placental malaria. Abdullahi et al.[41] found that *A. paniculata* is significantly effective against *Toxoplasma gondii* as compared to clindamycin and was safe for host cells. Apsari et al.[42] reported that the plant exhibits anti-parasitic effects by the following mechanisms, such as parasite suppression, immunomodulation, antioxidant activity, and inhibition of parasite invasion pathways. Halder et al.[43] revealed that the plant extract also possesses activity against *Giardia lamblia* trophozoites by damaging DNA and inducing oxidative-stress and cell cycle arrest.

Antidiarrheal and intestinal effects

Tyagi et al.[44] demonstrated in their study that the ethanolic extract of *A.paniculata* could promote an anti-inflammatory effect in the gut and reduce inflammatory factors such as cytokines and also promote gut homeostasis. Wu et al.[45] in their study revealed that the use of andrographolide promoted the prevalence of beneficial bacteria in the gut, which in turn promoted gut health and anti-inflammatory status, whereas the use of amoxicillin disturbed gut health and promoted the presence of pathogenic microorganisms, such as *E.coli, Klebsiella,* and *Shigella* species. A schematic representation of a plausible mechanism of action of andrographolide on bacteria is shown in Figure 3.

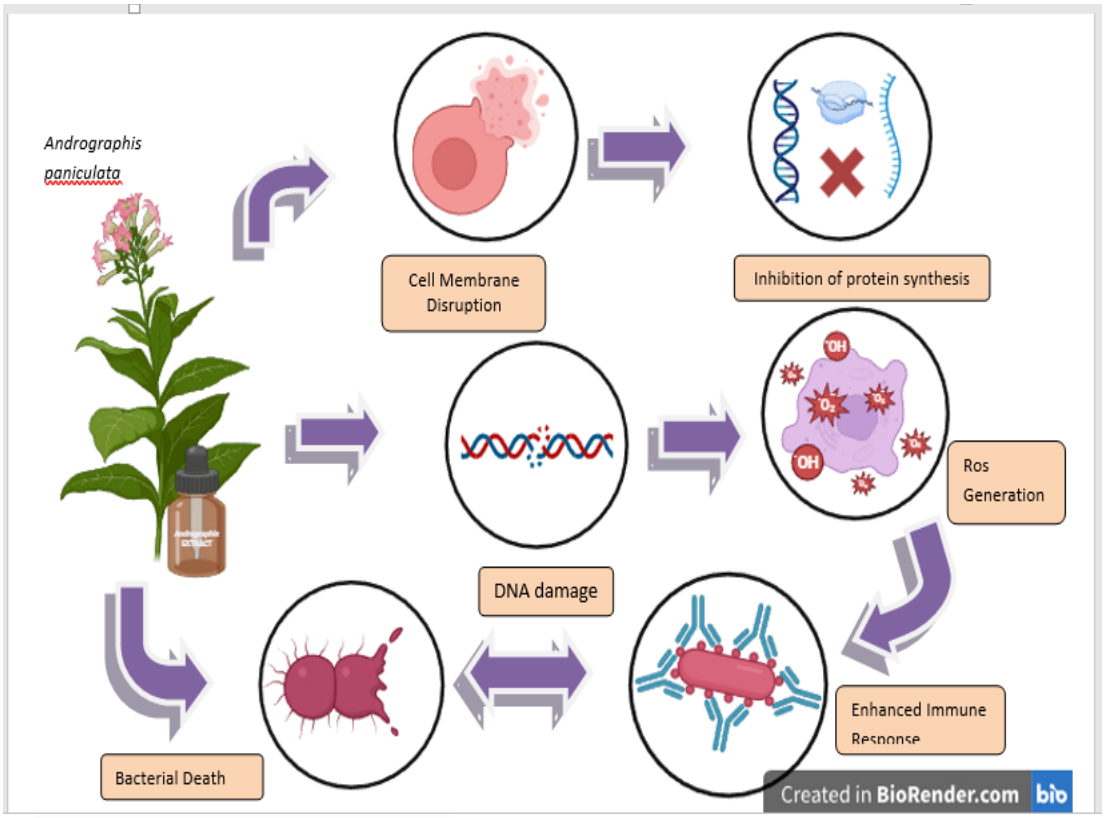

Figure 3. Schematic representation of mechanism of actions of andrographolide as antimicrobial

Antiviral effects

Andrographolide, derived from *A. paniculata,* and its natural and synthetic derivatives has been shown to possess anti-viral effects against HIV, HPV, influenza A, and others, by blocking viral entry, preventing viral replication and receptor binding.[46] The benzyl amino derivative of andrographolide shows anti-viral activity against influenza A virus subtype H3N2.[47] Paul et al.(48) in their in-silico and in-vitro study also revealed promising anti-dengue virus (DENV) activity. Both methanolic and acidic deep eutectic solvents (DES) have shown anti-viral activities against the human coronavirus HCoV-OC43.[49] Interestingly, in a study by Siridechakorn et al.,(50) the most potent anti-viral extract of the plant lacked andrographolide, whereas andrographolide-containing extracts showed moderate anti-viral activity.

Antifungal effects

Andrographis paniculata, due to its phytoconstituents, possesses strong anti-fungal activity.[51] The methanolic extract of the plant has been shown to inhibit mycelial growth and promote seed germination and seed growth in rice,[52] whereas the ethanolic extract at the highest concentration was more effective against dermatophytes, thus helping in various dermatomycoses.[53] Andrographolide also shows an additive or synergistic antifungal effect when combined with amphotericin B and also reduced drug-related toxicity, signifying its potential role in combination with standard drugs against clinically pathogenic fungi.[54] A study by Priya et al.(55) showed that *Andrographis paniculata* possesses docosahexaenoic acid and oleic acid which could inhibit the mycelial growth of *Collectrotrichum capsica.*

Anticancer activity

Arora et al. (56) in their study stated that in early times unmodified natural products were in use for developing drugs against cancer. Suriyo et al. (57) revealed that the plant extract along with andrographolide was shown to enhance the action of the anticancer drug 5-fluorouracil in HepG2 cells, but significantly altered CYP450 enzyme expression, particularly reducing CYP2D6, suggesting their cautious use. Malik et al.(58) stated that andrographolide has anti-cancer potential due to mechanisms such as apoptosis induction, cell cycle regulation, NF-κB suppression, and anti-angiogenic activity, but further clinical studies are required due to certain limitations, such as poor bioavailability and cytochrome P450 inhibition. According to Paul et al.,(59) the extract of *A. paniculata* could suppress HIF-1α and VEGF expression at both mRNA and protein levels by modifying the transcription factors, thus having an inhibitory effect on hypoxia-induced tumor angiogenesis. In cases of resistance to 5-fluorouracil by colorectal cancer, *Andrographis* can enhance the activity of 5-fluorouracil in resistant CRC cells, mouse xenografts, and patient-derived tumoroids by suppressing Dickkopf-1 (DKK1) overexpression and inhibiting Akt signaling.[60]

Antivenom effects

Prabhu et al.(61) demonstrated that *A. paniculata* extract along with reduced-dose (50 percent) anti-snake venom could lower the cardiotoxicity in rats induced by cobra venom than could anti-snake venom (ASV) alone. A study by Tan et.(62) al also showed that the dichloromethane root extract of *Andrographis paniculata* shows anti-venom activity by inhibiting secretory phospholipase A_2 ($sPLA_2$) from *Naja philippinensis* venom. A study by Nayak et al.(63) also revealed the anti-venom activity of *Andrographis paniculata* methanolic extract, and showing that the plant could be used as a supplement in addition to snake anti-venom. The plant extract also can potentially protect the brain from cobra venom, improve behavior, increase dopamine levels and reinstate the brain structure, than can anti-snake venom alone.(64)

Cardiovascular effects

Saraswati et al.(65) in their study revealed that *Andrographis paniculata* has potential cardioprotective effect, having several benefits for the heart such as reduced cardiac remodeling and hypertrophy, and help in improving the problem of myocardial infarction and diabetic cardiomyopathy. It also has potential antithrombotic effect, by inhibiting platelet aggregation through reduced thromboxane B2 (TXB2) levels and enhanced antithrombin III activity.(66) They prevent myocardial injury by anti-inflammatory, antioxidant, anti-apoptotic, and antifibrotic mechanisms. These effects are mediated through important signaling pathways which includes NF-κB, PI3K/Akt, MAPK, STAT3, Nrf2, IGF-1R, and PPAR-α.[67] The ethanolic extract of the plant also reduces Ang-II–induced cardiac hypertrophy in H9c2 cells. The

extract does so by reducing inflammation and oxidative stress by modifying Nrf2/NF-κB/NLRP3 signaling pathway.[68] It improves heart tissue structure, lowers cardiac injury markers, [69] and also protects the heart from injury caused by diclofenac in rats and potentially reduces harmful blood lipids.[70]

Controlled clinical trials of *A. paniculata* treatment

Our systemic investigation revealed a total of 24 individual clinical trials after removing the duplicates from three different databases. Wanaratna et al.(71) in their study stated that the baseline characteristics were comparable between *Andrographis paniculata* extract (APE) treatment and placebo-control groups. Patients receiving APE showed lower rates of SARS-CoV-2 compared to placebo (34.5% vs. 57.1%), while elevated CRP levels (>10 mg/L) were significantly less frequent in the APE group (0% vs. 17.9%). Pneumonia developed only in the placebo group (10.7% vs. 0%). Makmur et al.(72) observed that treatment with *A. paniculata* ethanolic extract in 250 mg capsules three times daily for five days demonstrated a high efficacy of 94.2% against *Plasmodium vivax*, *Plasmodium falciparum*, and mixed malaria infections. They also observed that there were no adverse effects during the treatment period. A study by Zeng et al. (73) stated that *Andrographis paniculata* is a widely used traditional Chinese medicinal herb that has andrographolide as its primary bioactive constituent. Andrographolide exhibits a wide range of pharmacological activities, including anti-inflammatory, antioxidant, anti-cancer, antimicrobial, and antihyperglycemic effects. A randomized three way cross-over study conducted on *Andrographis* against URIs at a single center, using dehydroandrographolide succinate (DAS) infusion at 80mg, 160mg and 320 mg, developed non-linear pharmacokinetic characteristics with no other side-effects except stomach-ache. [74] Another randomized trial was conducted where 10 mg/kg Xiyanping (XYP) injection was administered for 28 days where it was observed that it reduced the time for the relief of cough, fever eradication, and clearance of the virus.[75] A randomized double blind placebo controlled trial was conducted where KalmCold capsules containing 100 mg of active substances were administered after breakfast and dinner, twice daily for 5 days. It was concluded that the extract was 2.1 times more effective than placebo capsules. However, several side-effects were observed including vomiting, diarrhea, nausea or lethargy.(76)

CONCLUSION

Andrographis paniculata possesses numerous medicinal properties and has been traditionally used since ancient times for various therapeutic purposes. Andrographolide, the major bioactive constituent of the plant, exhibits a broad spectrum of pharmacological effects and has attracted the interest of many researchers. This review summarises all the important aspects of the plant, such as hepatoprotective effects, anti-inflammatory activities, antioxidant activities, anti-diabetic, anti-hyperlipidemic, antipyretic effects, antimicrobial, and anti-parasitic effects, antidiarrheal and intestinal effects, anticancer activity, antivenom effects, and cardiovascular effects. Other clinical evidence points to *A. paniculata* as a potential cure for acute upper respiratory tract infections (URIs) and HIV, and as a strong immune system stimulant. Although several clinical studies have been conducted, more research and development have to be done to further verify and exploit various other biological activities of the plant. Therefore, we anticipate that *Andrographis paniculata* could serve as a valuable complementary therapeutic agent in the treatment of various ailments.

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