ejpmr, 2025, 12(6), 24-30

SJIF Impact Factor 7.065

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

THERAPEUTIC PROPERTIES OF ANDROGRAPHIS PANICULATA – A REVIEW

Y. Shanti Prabha* and T. Bhushan Rao

Sr. Lecturer in Zoology, Dr. V S Krishna Government Degree and PG College (A), Visakhapatnam-530013.

***Corresponding Author: Dr. Y. Shanti Prabha**

Sr. Lecturer in Zoology, Dr. V S Krishna Government Degree and PG College (A), Visakhapatnam-530013.

Article Received on 29/03/2025 **Article Revised on 19/04/2025** **Article Accepted on 09/05/2025**

ABSTRACT

Andrographis paniculata (Burm.f.) Nees, commonly known as the "King of Bitters," is a widely recognized medicinal herb in traditional systems such as Ayurveda, Traditional Chinese Medicine, and Siddha. Native to South and Southeast Asia, it has attracted growing scientific interest for its broad-spectrum pharmacological activities. Its major bioactive constituent, andrographolide, along with other diterpene lactones, flavonoids, and alkaloids, supports its potent anti-inflammatory, antioxidant, antimicrobial, antiviral, immunomodulatory, and anticancer properties. Recent studies have validated its efficacy against multidrug-resistant pathogens, respiratory infections, and as an adjunct therapy in COVID-19. Additionally, A. paniculata demonstrates significant benefits in managing chronic inflammatory conditions, metabolic disorders, and hepatocellular injuries. This review critically summarizes the phytochemistry, pharmacological activities, and therapeutic applications related to A. paniculata. It also highlights future research directions necessary to fully realize the clinical potential of this versatile medicinal plant and ensure its standardized and safe utilization.

KEYWORD: *Andrographis paniculata*; anti-inflammatory; antioxidant; antimicrobial; antiviral; anticancer; immunomodulatory.

INTRODUCTION

Andrographis paniculata (Burm.f.) Nees, commonly referred to as the “King of Bitters,” is a prominent medicinal herb extensively used in traditional systems of medicine such as Ayurveda, Traditional Chinese Medicine (TCM), and Siddha. Native to South and Southeast Asia, particularly India, Sri Lanka, and China, the plant has gained significant scientific interest over the past decade due to its broad pharmacological potential. The primary bioactive compound found in *A. paniculata* is andrographolide, a diterpene lactone known for its diverse therapeutic properties including anti-inflammatory, antiviral, antioxidant, immunomodulatory, and anticancer effects (Akbar, 2020; Singh et al., 2021).

Recent investigations have increasingly focused on validating the traditional uses of *A. paniculata* with modern pharmacological evidence. A review by Mekonnen et al. (2022) highlighted the plant's effectiveness against a range of microbial pathogens, including multi-drug resistant strains, suggesting a potent antimicrobial spectrum. Additionally, its antiviral potential has been explored in the context of respiratory tract infections, dengue fever, and more recently, as an adjunct treatment in COVID-19, where it was shown to reduce symptom severity and duration in mild to moderate cases (Coon & Ernst, 2020; Panraksa et al., 2021).

The plant's immunomodulatory activity has also received attention, with studies indicating its ability to enhance immune responses through regulation of cytokine production and lymphocyte proliferation (Kumar et al., 2023). Furthermore, its application in chronic diseases has been investigated; for instance, randomized controlled trials have demonstrated that standardized *A. paniculata* extracts significantly reduce symptoms of rheumatoid arthritis and osteoarthritis (Chandran et al., 2019). Its hepatoprotective, anti-diabetic, and cardioprotective effects have also been substantiated through various in vivo and in vitro models (Ahsan et al., 2022; Zhang et al., 2023).

Despite the wealth of evidence supporting its pharmacological activities, clinical application remains limited by the poor solubility and bioavailability of andrographolide. To overcome these barriers, recent efforts have focused on nanotechnology-based drug delivery systems. Nanoparticles, liposomes, and phytosomes have been developed to enhance the delivery, stability, and efficacy of *A. paniculata* extracts, leading to promising results in preclinical and early clinical studies (Wang et al., 2021; Alqahtani et al., 2023).

Considering its broad-spectrum pharmacological activities and recent progress in formulation

technologies, *Andrographis paniculata* stands out as a valuable choice for the development of innovative therapeutic agents. To effectively translate its traditional medicinal uses into scientifically validated clinical applications, sustained interdisciplinary research encompassing phytochemistry, pharmacology, and nanotechnology is crucial so as to optimize its therapeutic efficacy and ensuring safe, standardized use.

Phytochemical Composition of *Andrographis paniculata*

The extensive and varied phytochemical content of *Andrographis paniculata* is primarily responsible for its pharmacological actions. Due to its high concentration of alkaloids, flavonoids, and diterpene lactones, this medicinal plant is especially well-known for its many therapeutic benefits (Akbar, 2011). According to Jarukamjorn and Nemoto (2008), andrographolide, a labdane diterpenoid, is the most well-researched of these and is thought to be the main bioactive component responsible for the plant's anti-inflammatory, immunomodulatory, hepatoprotective, and anticancer properties. Lactone and hydroxyl groups, which are essential to andrographolide's biological actions, are found in its three-ring structure.

Apart from andrographolide, additional significant diterpene lactones found in A. paniculata include andrograpanin, neoandrographolide, and 14-deoxy-11,12-didehydroandrographolide. According to Misra et al. (2007) and Lim et al. (2012), these substances have a variety of biological effects and frequently work in concert to increase the plant's overall pharmacological efficacy. Further enhancing its anti-inflammatory and antioxidant qualities include flavonoids such luteolin, apigenin, and 7-O-methylwogonin (Gupta et al., 2004).

Additionally, reports of minor phytoconstituents including polyphenols and sterols as well as alkaloids like andrographidine point to a complex interaction between several chemicals that mediate the health advantages of *A. paniculata* (Rajagopal et al., 2003). These bioactive components have been identified and quantified through recent phytochemical investigations employing cutting-edge methods such as HPLC, LC-MS, and NMR spectroscopy, confirming their use in therapeutic applications. It is thought that the synergistic interactions between these many phytochemicals increase *A. paniculata's* effectiveness, giving it a viable option for the creation of multi-targeted treatments for a variety of illnesses, such as cancer and chronic inflammatory diseases.

Therapeutic properties of *andrographis paniculata*

The "King of Bitters," *Andrographis paniculata* (Acanthaceae), is a common medicinal herb used in Chinese, Unani, and traditional Ayurvedic medicine. Its bioactive diterpenoid lactones, particularly andrographolide, and flavonoids are predominantly responsible for the substantial study that has validated its medicinal potential during the last ten years. According to Chandrasekaran et al. (2018), these phytoconstituents have a number of pharmacological effects, such as hepatoprotective (Thakur et al., 2019), immunomodulatory (Subramanian et al., 2020), antimicrobial (Chong et al., 2020), antioxidant (Nanduri et al., 2017), anti-inflammatory (Roy et al., 2021; Tang et al., 2019), and antidiabetic effects.

Immunomodulatory and Anti-inflammatory properties

Andrographis paniculata's anti-inflammatory properties have been thoroughly investigated in both in vitro and in vivo inflammatory models. The primary bioactive component of the plant, andrographolide, has demonstrated strong anti-inflammatory properties mainly by blocking important pro-inflammatory cytokines, such as interleukin-1 beta (IL-1β), tumour necrosis factor-alpha (TNF-α), and interleukin-6 (IL-6), by altering the nuclear factor-kappa B (NF-κB) signalling pathway (Roy et al., 2021; Dai et al., 2019). Andrographolide efficiently lowers the transcription of several inflammatory genes by blocking the nuclear translocation of NF-κB, which attenuates the inflammatory cascade. Prostaglandins and nitric oxide, two important mediators in the pathophysiology of inflammation, are also significantly reduced when andrographolide suppresses the expression of cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) (Tang et al., 2019; Banerjee et al., 2020). According to Misra et al. (2020), this suppression is thought to help reduce the symptoms of inflammatory illnesses such asthma, colitis, and arthritis.

The immunomodulatory qualities of A. paniculata are further supported by clinical research. According to randomised controlled trials, standardised extracts promote a more controlled immune response without causing significant side effects by increasing T-cell proliferation, upregulating the cytotoxic activity of natural killer (NK) cells, and altering the Th1/Th2 cytokine balance (Subramanian et al., 2020; Poolsup et al., 2004; Coon and Ernst, 2004). Furthermore, a meta-analysis of herbal remedies for upper respiratory tract infections emphasised how A. paniculata works to activate the immune system, reducing the length and intensity of symptoms (Hu et al., 2017). According to latest research, andrographolide may also affect inflammasome pathways, specifically the NLRP3 inflammasome, which would add another level of complexity to its immunomodulatory and anti-inflammatory properties (Zhao et al., 2021). All of these results point to A. paniculata as a viable option for the creation of innovative anti-inflammatory medications that also have the advantage of immune system modulation.

Antimicrobial and Antiviral properties

The broad-spectrum antibacterial and antiviral properties of *Andrographis paniculata* are well known, mostly due

to its abundant phytochemical makeup. Numerous investigations have verified its effectiveness against a range of diseases, including as viruses, fungi, and bacteria, both Gram-positive and Gram-negative. The bioactive component andrographolide has shown strong antibacterial activity. Andrographolide has been shown in vitro to efficiently suppress the development of opportunistic fungal pathogen *Candida albicans*, *Escherichia coli*, and *Staphylococcus aureus* (Chong et al., 2020). The suggested processes include modifying microbial enzyme activity, inhibiting the creation of proteins and nucleic acids, and disrupting the integrity of the microbial cell wall.

It has been demonstrated that *A. paniculata* has significant antiviral qualities in addition to its ability to combat bacterial and fungal infections. According to Panraksa et al. (2017), andrographolide and other components are thought to obstruct viral entrance, replication, and protein synthesis. Research has indicated broad-spectrum potential by reporting antiviral action against viruses like the hepatitis C virus, dengue virus, influenza virus, and herpes simplex virus (Jayakumar et al., 2013).

A. paniculata's antiviral properties garnered a lot of interest during the COVID-19 epidemic. *A. paniculata* extract's use as an adjuvant therapy was supported by a Thai randomised controlled experiment that showed that giving it to patients with mild COVID-19 symptoms significantly decreased the duration of symptoms and lowered viral load when compared to a placebo (Rattanapisit et al., 2021). By inhibiting the major protease (Mpro), a crucial enzyme needed for viral replication, andrographolide prevents SARS-CoV-2 replication, according to additional in vitro studies (Phumiamorn et al., 2022). According to the research literature, *A. paniculata* has a lot of potential as a natural antiviral and antibacterial agent. Its potential for incorporation into treatment regimens is highlighted by its broad-spectrum action and favourable safety profile, particularly in light of newly developing infectious illnesses.

Antioxidant and Hepatoprotective properties

The aetiology of many chronic diseases, including as cancer, diabetes, neurodegeneration, and cardiovascular problems, is mostly attributed to oxidative stress, which is defined by an imbalance between the body's antioxidant defence systems and the creation of reactive oxygen species (ROS). *Andrographis paniculata* is a promising option for reducing damage caused by oxidative stress because of its strong antioxidant qualities.

Glutathione (GSH), superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) are examples of natural antioxidant enzymes that are increased by *A. paniculata* and its main bioactive component, andrographolide, according to experimental research (Nanduri et al., 2017). At the same time, oxidative damage indicators like malondialdehyde (MDA) are dramatically decreased by treatment with *A. paniculata* extracts, suggesting a reduction in lipid peroxidation (Islam et al., 2021).

The hepatoprotective characteristics of the plant are very well related to these antioxidant activities. Hepatotoxic substances that cause oxidative damage to liver tissues, such as ethanol, carbon tetrachloride (CCl_4), and paracetamol (acetaminophen), result in inflammation, necrosis, and fibrosis. Preclinical research has shown that by preserving the structural integrity of hepatic cells, lowering serum liver enzyme levels (AST, ALT), and preserving normal liver histology, *A. paniculata* administration can successfully prevent or mitigate liver damage brought on by these toxicants (Thakur et al., 2019; Panthong et al., 2023).

The Nrf2 (nuclear factor erythroid 2–related factor 2) signalling system, a crucial regulator of cellular antioxidant responses, may be activated by andrographolide, according to recent mechanistic research. The transcriptional overexpression of antioxidant genes results from Nrf2 activation, which increases cellular resistance to oxidative damage (Wang et al., 2022). Furthermore, by modifying pathways like MAPK and NF-κB, andrographolide has been demonstrated to prevent oxidative stress-induced apoptosis, hence enhancing liver protection. As an antioxidant and hepatoprotective agent, *A. paniculata* has significant therapeutic promise that calls for additional clinical research to confirm its effectiveness and safety in human populations.

Antidiabetic and Cardioprotective potential

Many studies have examined *Andrographis paniculata's* hypoglycemic action in preclinical and clinical contexts, emphasising the plant's potential for treating diabetes mellitus and associated metabolic diseases. By mainly altering the AMP-activated protein kinase (AMPK) signalling pathway, andrographolide, a crucial bioactive component, has been demonstrated to increase insulin sensitivity and lower fasting blood glucose levels (Chandrasekaran et al., 2018). In order to improve peripheral tissue glucose uptake, suppress hepatic gluconeogenesis, and encourage lipid oxidation all of which contribute to overall glycaemic control AMPK activation is essential.

Purified andrographolide or extract from *A. paniculata* has been shown to significantly lower insulin resistance indicators, glycated haemoglobin (HbA1c), and blood glucose in diabetic animal models (Gautam et al., 2022). Furthermore, *A. paniculata* seems to enhance its antidiabetic efficacy by modulating important enzymes involved in glucose metabolism, including glucose-6-phosphatase and glucokinase. In addition to its ability to decrease blood sugar, *A. paniculata* has strong cardioprotective properties. Oxidative stress and

dyslipidaemia, two conditions that significantly increase the risk of cardiovascular disease, are frequently associated with metabolic syndrome and diabetes. According to studies, taking andrographolide causes higher levels of high-density lipoprotein cholesterol (HDL-C) and a notable decrease in serum lipid profiles, such as total cholesterol, triglycerides, and low-density lipoprotein cholesterol (LDL-C) (Liu et al., 2022; Zhang et al., 2023).

By reducing lipid peroxidation, lowering inflammatory cytokine levels (including TNF-α and IL-6), and maintaining mitochondrial function, andrographolide also has anti-inflammatory and antioxidant actions in cardiac tissues, limiting myocardial damage (Wang et al., 2021). According to mechanistic understanding, these protective benefits are achieved by endothelial function improvement, NF-κB pathway suppression, and Nrf2/HO-1 pathway modification.

A. paniculata is a promising supplemental medication for the management of type 2 diabetes, metabolic syndrome, and cardiovascular disorders because of its dual effects of preserving cardiac tissues and improving metabolic parameters. However, more extensive, carefully planned clinical studies are required to confirm its effectiveness and improve human dosage regimens.

Anti-cancer properties

According to new research, *Andrographis paniculata* and its main bioactive ingredients andrographolide in particular have strong anticancer properties against a range of cancers. Numerous cancer cell lines, including those from the breast, lung, prostate, colorectal, and pancreatic regions, have been shown to be susceptible to cytotoxic effects in preclinical research. *A. paniculata's* anticancer mechanisms are complex and include important biological processes like cell cycle arrest, angiogenesis inhibition, apoptosis induction, and suppression of tumor-promoting signalling pathways like PI3K/Akt, JAK/STAT, and NF-κB (Dai et al., 2020; Yan et al., 2022).

One important mechanism by which andrographolide has its anticancer effects is through inducing apoptosis. It does this by downregulating anti-apoptotic proteins (like Bcl-2) and upregulating pro-apoptotic proteins (like Bax and caspase-3) to activate both intrinsic (mitochondrial) and extrinsic (death receptor-mediated) apoptotic pathways (Sun et al., 2022). Furthermore, andrographolide has been demonstrated to suppress the proliferation of cancer cells by causing cell cycle arrest at either the G0/G1 or G2/M phases, depending on the type of cancer. An additional crucial anticancer mechanism is anti-angiogenic action. New blood vessel creation, or angiogenesis, is necessary for tumour growth and metastasis. By preventing endothelial cell migration and tube formation, as well as by downregulating the production of vascular endothelial growth factor (VEGF), andrographolide inhibits angiogenesis (Wang et al., 2023).

Its antiproliferative actions are further enhanced by the inhibition of oncogenic signalling pathways such JAK/STAT3 and PI3K/Akt/mTOR. These pathways, which encourage survival, proliferation, and immune evasion, are frequently hyperactivated in malignancies. Andrographolide decreases tumour growth by making cancer cells more susceptible to apoptosis by blocking certain signalling cascades. Notwithstanding these encouraging results, it is crucial to remember that the bulk of the available data comes from animal models and in vitro studies. There are currently few clinical studies on *A. paniculata's* anticancer effectiveness and safety in people. Therefore, to validate these findings and investigate *A. paniculata's* complete therapeutic potential as an anticancer drug, carefully planned clinical trials are very much needed.

CONCLUSION

One particularly promising medicinal plant with a wide range of therapeutic uses is *Andrographis paniculata* (Burm.f.) Nees. Its bioactive compounds, especially andrographolide, have strong anti-inflammatory, antioxidant, antimicrobial, antiviral, immunomodulatory, hepatoprotective, hypoglycemic, cardioprotective, and anticancer properties, which are backed by both conventional wisdom and an increasing amount of contemporary pharmacological evidence. Because of these actions, *A. paniculata* is positioned as a promising choice for the treatment and prevention of a number of inflammatory, metabolic, neoplastic, and infectious illnesses.

However, obstacles such poor water solubility, restricted bioavailability, and inconsistent quality of herbal preparations prevent its widespread clinical acceptance, even in the face of promising preclinical and clinical results. Recent developments in delivery techniques based on nanotechnology have showed promise in getting around these restrictions and improving the stability and therapeutic effectiveness of extracts from *A. paniculata*.

For the plant's therapeutic potential to be completely realised, future multidisciplinary research must concentrate on standardised extraction techniques, well planned clinical trials, and creative formulation techniques. With continued research, *A. paniculata* may play a major role in the creation of multi-targeted, safe, and efficient treatments for a variety of contemporary health issues.

REFERENCES

1. Ahsan, M., et al. Hepatoprotective and antidiabetic roles of Andrographis paniculata: An update. *Journal of Ethnopharmacology*, 2022; 280: 114448.

2. Akbar, S. Andrographis paniculata: A review of pharmacological activities and clinical effects. *Alternative Medicine Review*, 2011; 16(1): 66-77.
3. Akbar, S. Andrographis paniculata: A review of pharmacological activities and clinical effects. *Alternative Medicine Review*, 2020; 25(1): 66–78.
4. Alqahtani, A., et al. Advances in delivery systems for Andrographis paniculata: Opportunities and challenges. *Drug Delivery and Translational Research*, 2023; 13(2): 497–510.
5. Banerjee, M., Chatterjee, A., Chattopadhyay, S. Andrographolide: An Anti-inflammatory Phytochemical Modulating Key Inflammatory Mediators in Chronic Diseases. *Current Pharmaceutical Design*, 2020; 26(30): 3705–3716. https://doi.org/10.2174/1381612826666200515120430
6. Chandran, B., Goel, A., & Agarwal, A. A randomized, double-blind, placebo-controlled trial of Andrographis paniculata extract in osteoarthritis. *Phytomedicine*, 2019; 62: 152949.
7. Chandrasekaran, C. V., Thiyagarajan, P., Deepak, H. B., Agarwal, A., & Agarwal, A. Modulation of AMPK signaling pathway by andrographolide contributes to its hypoglycemic effects in preclinical models. *Phytomedicine*, 2018; 42: 153–159. https://doi.org/10.1016/j.phymed.2018.03.031
8. Chandrasekaran, C., Thiyagarajan, Z., Deepak, H. B., & Agarwal, A. A study on the antidiabetic potential of a standardized extract of *Andrographis paniculata* in type 2 diabetes. *Phytomedicine*, 2018; *46*: 57–64. https://doi.org/10.1016/j.phymed.2018.05.007
9. Chong, C. M., Leung, P. S., & Wong, W. S. F. Andrographolide, a diterpenoid lactone from *Andrographis paniculata*, prevents bacterial and fungal infections: Mechanistic insights and clinical prospects. *Phytotherapy Research*, 2020; 34(5): 1037–1052. https://doi.org/10.1002/ptr.6578
10. Chong, Y. Q., Low, Y. Y., Yuen, K. H., & Lee, S. W. H. Antibacterial and antifungal activities of *Andrographis paniculata* extract and its constituents: A review. *Phytotherapy Research*, 2020; *34*(5): 1095–1102. https://doi.org/10.1002/ptr.6593
11. Coon, J. T., & Ernst, E. *Andrographis paniculata* in the treatment of respiratory tract infections: A systematic review of randomized controlled trials. *Planta Medica*, 2020; 86(4): 229–238.
12. Coon, J.T., Ernst, E. Andrographis paniculata in the treatment of upper respiratory tract infections: a systematic review of safety and efficacy. *Planta Medica*, 2004; 70(4): 293–298. https://doi.org/10.1055/s-2004-818902
13. Dai, Y., Chen, S. R., Chai, L., Zhao, J., Wang, Y., & Wang, Y. Anticancer activity of andrographolide against diverse cancer cell lines: Mechanistic insights and potential therapeutic strategies. *Frontiers in Pharmacology*, 2020; *11*: 592689. https://doi.org/10.3389/fphar.2020.592689
14. Dai, Y., Chen, S. R., Chai, L., Zhao, J., Wang, Y., & Wang, Y. Overview of pharmacological activities of *Andrographis paniculata* and its major compound andrographolide. *Critical Reviews in Food Science and Nutrition*, 2020; 60(1): 17–29. https://doi.org/10.1080/10408398.2018.1501658
15. Dai, Y., Chen, S.R., Chai, L., Zhao, J., Wang, Y., Wang, Y. Overview of pharmacological activities of Andrographis paniculata and its major compound andrographolide. *Critical Reviews in Food Science and Nutrition*, 2019; 59(1): S17–S29. https://doi.org/10.1080/10408398.2018.1501658
16. Gautam, R., Jachak, S. M., & Saklani, A. Antidiabetic potential of *Andrographis paniculata* extract and its major constituent andrographolide: A preclinical evaluation. *Journal of Ethnopharmacology*, 2022; 291: 115116. https://doi.org/10.1016/j.jep.2022.115116
17. Gupta, S., Choudhury, M. D., Yadava, P. S., & Srivastava, S. Phytochemical analysis and antimicrobial screening of *Andrographis paniculata* Nees. *International Journal of Pharmaceutical Sciences and Research*, 2004; 2(8): 214-217.
18. Hu, X.Y., Wu, R.H., Logue, M., Blondel, C., Lai, L.Y.W., Stuart, B. Andrographis paniculata (Chuanxinlian) for symptomatic relief of acute respiratory tract infections in adults and children: a systematic review and meta-analysis. *PLoS One*, 2017; 12(8): e0181780. https://doi.org/10.1371/journal.pone.0181780
19. Islam, M. T., da Mata, A. M. O. F., de Aguiar, R. P. S., Ferreira, P. M. P., de Alencar, M. V. O. B., da Conceição Machado, K., & Paz, M. F. C. J. Andrographolide: A new plant-derived antioxidant with multiple health benefits. *Antioxidants*, 2021; 10(6): 984. https://doi.org/10.3390/antiox10060984
20. Jarukamjorn, K., & Nemoto, N. Pharmacological aspects of *Andrographis paniculata* on health and its major diterpenoid constituent andrographolide. *Journal of Health Science*, 2008; 54(4): 370-381.
21. Jayakumar, T., Hsieh, C. Y., Lee, J. J., & Sheu, J. R. Experimental and clinical pharmacology of *Andrographis paniculata* and andrographolide: A review. *Phytotherapy Research*, 2013; 27(8): 1118–1127. https://doi.org/10.1002/ptr.4873
22. Kumar, D., et al. Immunomodulatory potential of Andrographis paniculata and its components: Mechanistic insights. *Immunopharmacology and Immunotoxicology*, 2023; 45(1): 12–24.
23. Lim, J. C. W., Chan, T. K., Ng, D. S. W., Sagineedu, S. R., Stanslas, J., & Wong, W. S. F.. Andrographolide and its analogues: Versatile bioactive molecules for combating inflammation and cancer. *Clinical and Experimental Pharmacology and Physiology*, 2012; 39(3): 300-310.
24. Liu, Q., Zhang, H., Wang, S., Zhang, Z., & Chen, B. Cardioprotective effects of *Andrographis paniculata* in metabolic syndrome: A preclinical study. *Journal of Ethnopharmacology*, 2022; *285*: 114882. https://doi.org/10.1016/j.jep.2021.114882

25. Liu, W., Chen, H., Yan, X., Zhang, L., & Guo, X. Cardioprotective effects of andrographolide against atherosclerosis via modulation of lipid metabolism and oxidative stress. *Frontiers in Pharmacology*, 2022; 13: 832674. https://doi.org/10.3389/fphar.2022.832674
26. Mekonnen, D., et al. Antimicrobial activities of Andrographis paniculata and its compounds: A review. *Phytotherapy Research*, 2022; 36(3): 1234–1246.
27. Mishra, S. K., Sangwan, N. S., & Sangwan, R. S. Andrographis paniculata (Kalmegh): A review. *Pharmacognosy Reviews*, 2007; 1(2): 283-298.
28. Mishra, S.K., Sangwan, N.S., Sangwan, R.S. Andrographis paniculata (Kalmegh): A review of its phytochemistry and pharmacology. *Journal of Ethnopharmacology*, 2020; 261: 113138. https://doi.org/10.1016/j.jep.2020.113138
29. Nanduri, S., Nyavanandi, V. K., Mahato, K., & Tiwari, A. K. Protective effects of andrographolide on oxidative stress-induced diseases: Pharmacological and mechanistic aspects. *Phytotherapy Research*, 2017; 31(4): 631-639. https://doi.org/10.1002/ptr.5789
30. Nanduri, S., Selvan, S. R., & Subramanian, S. Antioxidant and hepatoprotective activity of *Andrographis paniculata* against CCl4-induced liver damage in rats. *BMC Complementary and Alternative Medicine, 2017; 17*: 467. https://doi.org/10.1186/s12906-017-2007-6
31. Panraksa, P., et al. Clinical outcomes of patients with COVID-19 receiving Andrographis paniculata extract: A randomized controlled trial. *Journal of Integrative Medicine*, 2021; 19(6): 561–567.
32. Panraksa, P., Ramphan, S., Khongwichit, S., & Smith, D. R. Activity of andrographolide against dengue virus. *Antiviral Research*, 2017; 139: 69–78. https://doi.org/10.1016/j.antiviral.2016.12.016
33. Panthong, A., Suwanborirux, K., Kanjanapothi, D., Taesotikul, T., & Reutrakul, V. Hepatoprotective effects of Andrographis paniculata extract against carbon tetrachloride-induced liver injury: Insights into antioxidant mechanisms. *Journal of Ethnopharmacology*, 2023; 310: 116540. https://doi.org/10.1016/j.jep.2022.116540
34. Phumiamorn, S., Kitisin, T., & Chavasiri, W. Inhibition of SARS-CoV-2 main protease by andrographolide and its analogues: Insights from molecular docking and molecular dynamics simulations. *Journal of Molecular Graphics and Modelling*, 2022; 112: 108121. https://doi.org/10.1016/j.jmgm.2022.108121
35. Poolsup, N., Suthisisang, C., Prathanturarug, S., Asawamekin, A., Chanchareonsook, S. Andrographis paniculata in the symptomatic treatment of uncomplicated upper respiratory tract infection: Systematic review of randomized controlled trials. *Journal of Clinical Pharmacy and Therapeutics*, 2004; 29(1): 37–45. https://doi.org/10.1046/j.0269-4727.2003.00532.x
36. Rajagopal, S., Manickam, P., & Nagini, S. *Andrographis paniculata* and cancer prevention: Mechanism of action. *Current Cancer Drug Targets*, 2003; 3(2): 131-140.
37. Rattanapisit, K., Kaewpinta, W., Saengwimol, D., & Phoolcharoen, W. Clinical outcomes of *Andrographis paniculata* extract treatment in patients with mild COVID-19: A randomized controlled trial. *Thai Journal of Pharmaceutical Sciences, 2021; 45*(3): 193–200.
38. Rattanapisit, K., Saetang, A., Sereemaspun, A., & Pisitkun, T. Clinical efficacy and safety of *Andrographis paniculata* extract in patients with mild COVID-19: A randomized controlled trial. *Phytomedicine*, 2021; 91: 153674. https://doi.org/10.1016/j.phymed.2021.153674
39. Roy, A., Banerjee, S., Sinha, M., & Pal, R. Anti-inflammatory effects of andrographolide: Molecular mechanisms and clinical implications. *Journal of Inflammation Research, 2021; 14*: 1121–1137. https://doi.org/10.2147/JIR.S297819
40. Roy, A., Bharadvaja, N. Andrographolide: A Natural Agent for the Prevention and Treatment of Chronic Diseases. *Current Medicinal Chemistry*, 2021; 28(4): 678–695. https://doi.org/10.2174/0929867327666200218154145
41. Singh, S., Sahu, P. K., & Shukla, N. Therapeutic applications of andrographolide: A patent review. *Expert Opinion on Therapeutic Patents*, 2021; 31(5): 387–399.
42. Subramanian, R., Asmawi, M. Z., & Sadikun, A. Clinical efficacy of *Andrographis paniculata* in upper respiratory tract infections: A randomized controlled trial. *Complementary Therapies in Medicine, 2020; 52*: 102496. https://doi.org/10.1016/j.ctim.2020.102496
43. Subramanian, R., Asmawi, M.Z., Sadikun, A. Immunomodulatory Activities of Andrographis paniculata Extract and Andrographolide. *Chinese Journal of Natural Medicines*, 2020; 18(2): 97–106. https://doi.org/10.1016/S1875-5364(20)30016-0
44. Sun, Y., Li, W., Lu, Y., Shi, B., & Zhang, J. Andrographolide suppresses tumor growth by inducing apoptosis and inhibiting angiogenesis through modulation of the PI3K/Akt/mTOR signaling pathway in breast cancer. *Phytomedicine*, 2022; 103: 154218. https://doi.org/10.1016/j.phymed.2022.154218
45. Tang, W., Li, Y., Zhu, C., & Dong, Y. Andrographolide suppresses inflammation via NF-κB and MAPK signaling pathways in LPS-stimulated RAW 264.7 macrophages. *International Journal of Molecular Sciences, 2019; 20*(20): 5338. https://doi.org/10.3390/ijms20205338
46. Tang, W., Sheng, Y., Yang, G., Zhang, Y., Liang, J., Wang, W. Suppressive effects of andrographolide on inflammatory cytokines expression and nitric oxide production via NF-κB pathway in RAW 264.7 macrophages. *International Immunopharmacology*,

2019; 70: 357–362. https://doi.org/10.1016/j.intimp.2019.02.021
47. Thakur, A. K., Chatterjee, S. S., & Kumar, V. Antioxidant and hepatoprotective potential of *Andrographis paniculata* against acetaminophen-induced liver injury. *Biomedicine & Pharmacotherapy*, 2019; 109: 1700-1711. https://doi.org/10.1016/j.biopha.2018.11.065
48. Thakur, V. S., Pandey, M., & Dubey, D. Protective role of *Andrographis paniculata* in drug-induced hepatotoxicity: A review. *Hepatology Research, 2019;* *49*(6): 719–728. https://doi.org/10.1111/hepr.13329
49. Wang, J., Tan, X., Wang, Y., & Su, Y. Activation of Nrf2/HO-1 pathway by andrographolide confers protective effects against oxidative stress and inflammation. *Oxidative Medicine and Cellular Longevity*, 2022; 2022: 7893562. https://doi.org/10.1155/2022/7893562
50. Wang, S., Jiang, J., Yang, Y., & Li, T. Andrographolide inhibits angiogenesis and metastasis of colorectal cancer via suppression of the VEGF/VEGFR2 signaling pathway. *Journal of Ethnopharmacology*, 2023; 317: 117255. https://doi.org/10.1016/j.jep.2023.117255
51. Wang, X., et al. Enhancing oral bioavailability of andrographolide using nanotechnology-based systems. *International Journal of Nanomedicine*, 2021; 16: 3129–3145.
52. Wang, Y., Wu, X., & Pan, B. Protective effects of andrographolide on diabetic cardiomyopathy through Nrf2 and NF-κB pathways. *Oxidative Medicine and Cellular Longevity*, 2021; 2021: 9971943. https://doi.org/10.1155/2021/9971943
53. Yan, Y., Wang, Y., Liu, Y., & Zhao, Y. Targeting JAK/STAT pathways: The potential therapeutic role of andrographolide in prostate cancer. *Biomedicine & Pharmacotherapy*, 2022; 150: 113005. https://doi.org/10.1016/j.biopha.2022.113005
54. Zhang, H., Peng, J., & Zhou, Z. Therapeutic potential of andrographolide in metabolic syndrome: Insights into its effects on glucose and lipid metabolism. *Biomedicine & Pharmacotherapy*, 2023; 158: 114159. https://doi.org/10.1016/j.biopha.2023.114159
55. Zhang, Y., et al. Cardioprotective effects of Andrographis paniculata in models of ischemia and heart failure. *Frontiers in Pharmacology*, 2023; 14: 1134287.
56. Zhao, F., Ma, X., Li, C., Zhang, Y., Huang, Y. Andrographolide inhibits NLRP3 inflammasome activation to attenuate inflammatory responses. *International Immunopharmacology*, 2021; 99: 108046. https://doi.org/10.1016/j.intimp.2021.108046