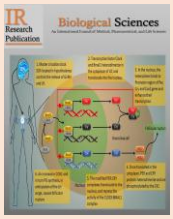
REVIEW ARTICLE

Biological Sciences
(An International Journal of Medical, Pharmaceutical, and Life Sciences)

Journal home: https://irrespub.com/biolsciences/index.php/1/index



A review on Pharmacological Activities of *Andrographis paniculata*

Shweta Parihar*

Department of Pharmacognosy, Maharshi Dayanand University, Near Delhi Bypass, Rohtak, Haryana-124001, India.

ARTICLE HISTORY

Received: 04-01-2022
Revised: 26-02-2022
Accepted: 06-03-2022
Online: 11-03-2022

KEYWORDS

Andrographis paniculata
Hepatoprotective
Anti-inflammatory activity
Pharmacology

ABSTRACT

Andrographis paniculata, is a very famous herbal plant belonging to the family Acanthaceae that has been used since ancient times. *Andrographis paniculata*, is also called Kalmegh and 'King of Bitters'. *Andrographis paniculata*, has been officially mentioned in Indian Pharmacopoeia It is a chief constituent of many Ayurvedic, Siddha, Unani, formulations which are used in the management of liver-related issues. It is a common herbal medicine used to treat snake and bug bites, diabetes, dysentery, fever, and malaria, abortifacient, cancer lytic, depurative, expectorant, hepatoprotective, hypoglycemic, immune enhancement, laxative, sedative, thrombolytic, vermicide, analgesic, antibacterial, antiperiodic, antipyretic, antithrombotic, antiviral. The present review article focuses on the pharmacological activities of *Andrographis paniculata*.

Introduction

A wide variety of therapeutic plants can be found all over the world. Many weeds in our environment are highly effective medicinal plants that can help with a variety of significant health issues (13,30,31,32,33). India has long been known as a great store of natural remedies among ancient cultures (34,48,35,36).

**Address for correspondence*
Department of Pharmacognosy, Maharshi Dayanand University, Near Delhi Bypass, Rohtak, Haryana-124001, India.
Email: shwetaparihar2502@gmail.com

DOI: http://dx.doi.org/10.55006/biolsciences.2022.2106
Published by IR Research Publication;

Andrographis paniculata is a well-known medicinal plant from the Acanthaceae family that has been utilized since antiquity. Kalmegh and 'King of Bitters' are two names for *Andrographis paniculata*. *Andrographis paniculata* has been formally included in the Indian Pharmacopoeia. It is a key ingredient in many Ayurvedic, Siddha, and Unani formulations for the treatment of liver problems (1). It is a common herbal medicine used to treat snake and bug bites, diabetes, dysentery, fever, and malaria, as well as abortifacient, cancer lytic, depurative, expectorant, hepatoprotective, hypoglycaemic, immune enhancement, laxative, sedative, thrombolytic, vermicide, analgesic, antibacterial, antiperiodic, antipyretic, antithrombotic, antiviral (5,62). Andrograpanin, andrographolide (2.39 percent), paniculide-A, paniculide-B, paniculide-C, 14-deoxy-11-dehydroandrographolide, 5-hydroxy-7,8,2',3'-tetramethoxyflavone, neoandrographolide, paniculide-D, paniculide-E, paniculide-F (3,4,62). The present review article focus on the pharmaco-

-logical activities of *Andrographis paniculata*. There are many species of Andrographis some of the names are:- *Andrographis paniculata*; *Andrographis affinis*; *Andrographis alataa* [vahl] Nees; *Andrographis atropurpurea* [Dennst] Alston; *Andrographis beddomeii*; *Andrographis ceylanica* Nees; *Andrographis ceylanica* Wight; *Andrographis chendurunii*; *Andrographis echioides* Nees; *Andrographis elongate* [Vahl]; *Andrographis explicate* (C.B.Clarke) Gamble; *Andrographis glanduloosa* Nees; *Andrographis glomeruliflora* Bremek; *Andrographis gracilis* Nees; *Andrographis humifusa* Wall.ex Nees; *Andrographis hygrophiloides*; *Andrographis lawsonii*.

Pharmacological activities

Anti-inflammatory activity

Andrographolide was determined to inhibit the inflammatory responses produced with the aid of rat neutrophils. The N-formyl-methionyl-leucyl-phenylalanine (fMLP)- neutrophil incited adhesion and transmigration in a concentration-dependent manner can be prevented by andrographolide (59). The pre-treatment of andrographolide decreased the H2O2 and o2 production which is increased by FMLP. It also decreases the CD11 and CD18 which are increased by FMLP. The study demonstrated that andrographolide reduced the reactive oxygen species (ROS) production with the help of modulation of protein kinase C-dependent pathway. It affected the regulation of Mac-1, which is crucial for neutrophil adhesion and transmigration (41). The activated kappa B was inhibited, in humans, fibroblast COX-2 is present which is inhibited and nitric oxide synthase (iNOS) was suppressed (10,11,12,14,15). In mice, andrographolide reduced the chances of peritoneal inflammation, the peritoneal inflammation is caused by acetic acid production. It indicated its ability to inhibit the permeability of small blood vessels. Eicosanoids and platelet-activating factor (PAF) are examples of inflammatory mediators which were also affected by the andrographolide in a manner of dose-dependent (IC50 ~ 5 μM) (4). In mice lungs which are infected with pathogenic influenza viruses, H5N111 14-Deoxy-11,12-didehydroandrographolide, inhibited the pro-inflammatory cytokines/chemokines (TNF-α, IL-1β, IL-6, CCL-2/MCP-1, IFN-α, IFN-β, IFN-γ, MIP-1α, MIP-1β40,41,42. **Figure 2** shows the role of andrographolide as an anti-inflammatory agent.

Neuroprotective activity

RSC96 cells in the in vitro conditions, when treated with andrographolide, show the neuroprotective effect. The RSC96 cells are similar to rat Schwann cell lines. The Schwann cell lines were treated with a different concentration range of andrographolide i.e 0 to 5 uM by MTT assay. The dose of 0.78 and 12.5 uM of andrographolide was effective. The dose is assayed based on the synthesis, morphology of cells, cell proliferation, genes that are specific to nerves. The DNA content was increased by this assay. This assay also helps to increase the glial cells lines, brain, ciliary which were derivatives of neurotrophic factors and Schwann cell markers. Andrographolide slowed down the further growth of RSC96 cells without changing the phenotype of Schwann cells (52,38). Andrographolide therapeutically increased the heme oxygenase-1 i.e HO-1 amount in astrocytes and NF-E2-related factor 2. Heme oxygenase-1 is a gene that targeted the factor Nrf2 (transcription factor). It also protects from oxidative stress in cellular defense (51). Andrographolide cures the cognitive impairment in Octodon degus. Octodon degus is a type of wild rodent species is found in South America. Octodon degus suffer from Alzheimer's like diseases with age. Andrographolide treatment shows the recovery in the transmission of synaptic basal, learning memory, spatial memory. Andrographolide treatment protects synaptic proteins and reduced the maturation of amyloid-beta aggregation and phosphorylated tau proteins in aged Octodon degus (39). **Figure3** shows the role of andrographolide as a neuroprotective agent.

Antioxidant activity

The 50 % hydro methanolic extract of *Andrographis paniculata* stops the leakage of lactate dehydrogenase in the heart. This extract also cures the heat of myocardial ischemic injury which is induced by the isoproterenol. The concentration of 100 mg/ml of hydro methanol extract shows H202, linoleate free radicals, and DPPH scavenging activity. The leaves, stems, roots, and fruits ethanolic extract dose 10 mg/ml of *Andrographis paniculata* were studied for the antioxidant activity on superoxide dismutase assay, free radical scavenging assay, and red cell hemolysis assay. Fruit ethanolic extract shows the high DPPH scavenging assay with 88.13% and leaf ethanolic extract shows the antioxidant activity (37).

Anticancer Activity

Andrographolide contains many anticancer activities. It stops the activity of A549 cells by reducing P13/Akt signal and inactivating c-jun/c-Fos and MMP-7 expression (21). Andrographolide with a combination of conventional chemotherapeutic agents is also used in cancer treatments for example combination of doxorubicin with andrographolide increase the chemosensitivity of tumor cells and

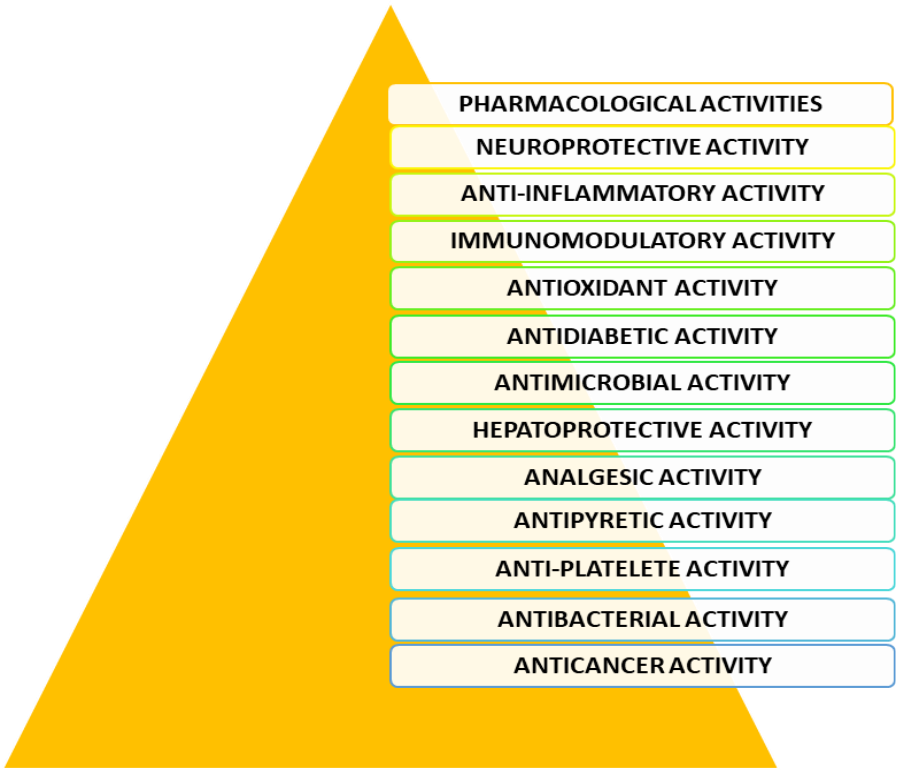


Fig 1. Pharmacological activities of *Andrographis paniculata*.

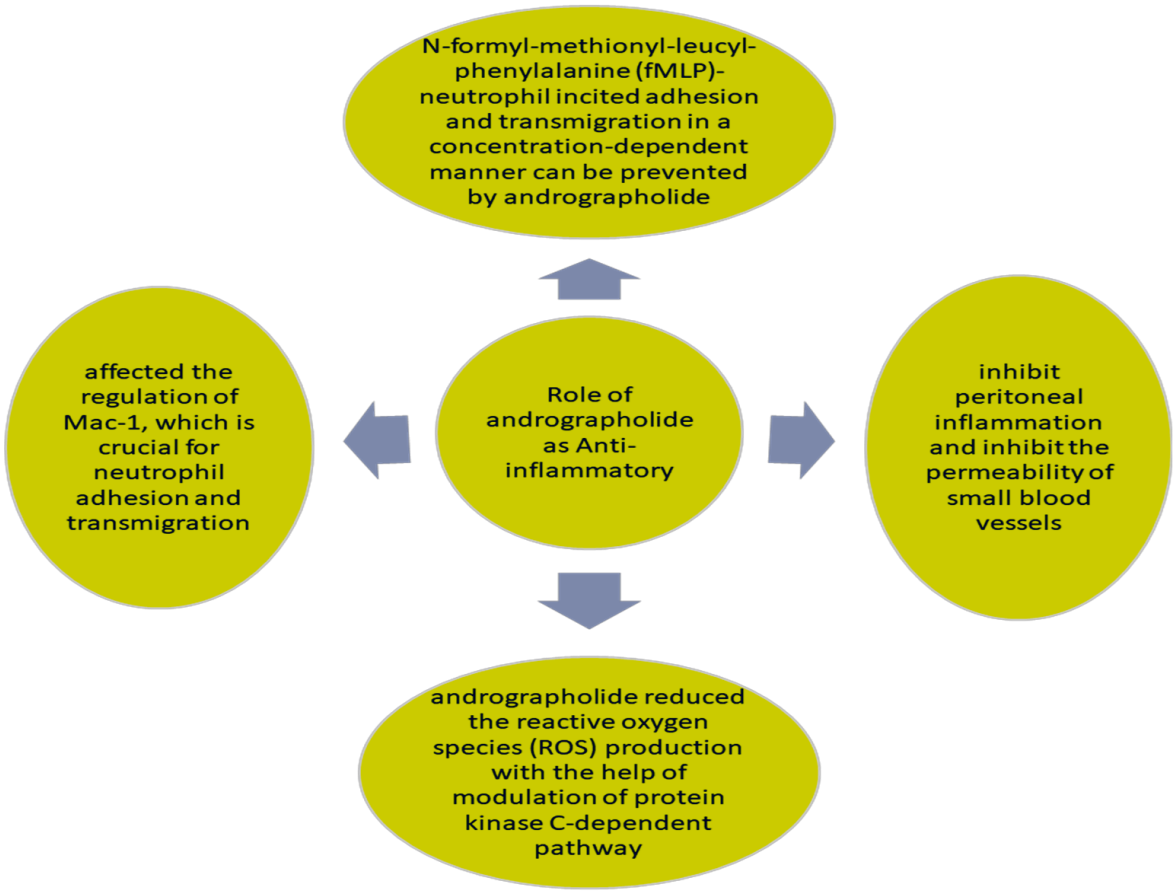


Fig 2. Role of andrographolide as Anti-inflammatory.

stop the activity of STAT3 activity (58). Andrographolide stops the growth of in-vitro and in-vivo DU145 cells by suppressing the IL-6 signal path (29). Andrographolide also helps in triggering apoptosis. Andrographolide also helps in increasing the cell cycle arrest (21). Andrographolide stops the growth of prostate cancer cells and androgen receptors. Andrographolide inhibits androgen receptors expression at the site of a protein, mRNA levels, transactivated targeted genes, nuclear translocation, inhibit Hsp90 binding on androgen receptors, which resulted in degradation of proteasome-mediated androgen receptors. Andrographolide stops the growth of C4-2 cells by decreasing the activity of androgen receptors. Androgen targeted genes like prostate-specific antigens i.e PSA is also inhibited by andrographolide (60). Andrographolide dose 10mg/kilogram was found to inhibit the growth of hepatoma tumor in vivo in xenograft species of mice. The chip analysis of 22 miRNAs decreases in 10 miRNAs number after the treatment. The miRNAs help in knowing that a major quantity of genes were involved in signal pathways for example miRNAs involved in cancer, focal adhesion, and MAPKs i.e mitogen-activated protein kinases (23). Yan et al. in 2012 had demonstrated the cytotoxic effects in human T-ALL i.e T-cell acute lymphoblastic leukemia through andrographolide. The dose of 10 ug/ml of andrographolide increases the apoptosis of Jurkat cells by inhibiting the pathway of P13K/AKT. Paclitaxel and Andrographolide combination show synergistic effects against cancer. This combination study was done against non-small cell lung cancer i.e A549 NSCLC cells. This study involved 0.48-60.75 nM dose of paclitaxel, 5.10-328.0 uM dose of andrographolide is treated for 24 to 48 hours on ROS reactive intracellular oxygen species and cell cycle, proliferated cells, and apoptosis. 100 microgram per kilogram Andrographolide and 20 microgram per kilogram of paclitaxel show antitumor activity on xenograft murine model. The combination of paclitaxel and Andrographolide have a 98 percent chance to stop the growth of odd A549 tumor (55). Andrographolide showed an inhibitory effect on MDA-MB-231 breast cancer cells. The prolonged use of Andrographolide increased the number of apoptotic cells. Andrographolide induced the production of extracellular reactive oxygen species i.e ROS and MMP i.e mitochondrial membrane potential production is reduced. The externalization of phosphatidylserine occurred. The cells which were treated with Andrographolide activated the caspase 3, caspase9, bax, apaf-1. Bcl-2 and Bcl-xl were reduced Andrographolide was also used to stop prostate cancer. Andrographolide targeted the regulators of the cell cycle, CXCR3, and CXCR7 (27).

14-Deoxy-11,12-didehydroandrographolide increases the production of autophagosomes and endoplasmic reticulum (ER) vacuoles. It increases the LC3-II in cells of breast cancer. It makes a large amount of cytosolic calcium concentration which leads to the breaking of mitochondrial membrane potential in LC3-II cells. DDIT3 suppressed the production of autophagosomes and endoplasmic reticulum (ER). The autophagosomes are depended on the transcription process. 14-DDA-increased the stress levels of the endoplasmic reticulum (ER). Gao et al. has demonstrated that andrographolide stops the growth of multiple myelomas cells. It shows the activity on nuclear factor i.e NF-kB signaling pathway (16). Colon cancer (HT-29) can be inhibited by the dichloromethane fraction of AP. Human peripheral blood lymphocytes proliferation can also be inhibited by the dichloromethane fraction of AP. Andrographolide inhibited many cancers like melanoma M14, central nervous system U251, lung H522, prostate DU 145, breast NCI/AD-RES, colon SW620 (20). The AP ethanol extract shows in vivo and in vitro inhibitory activity on AOM i.e azoxymethane-induced ACF i.e aberrant crypt foci in rats. PCNA proliferating cell nuclear antigens and beta-catenin protein were reduced by the AP treatment (2). Andrographolide when interacted with BAX then it protects BAX from degradation and increases the apoptosis caused by mitochondrial-mediated. In colorectal cancer in vivo models and in vitro models were studied with andrographolide. Combinational treatment of 5-Fluorouracil and andrographolide increase the apoptosis level of BAX and HCT116/5-fluorouracil (50). Andrographolide methanol extract was divided into various parts and these parts are mixed with different solvents then these were analyzed for oral squamous carcinoma cell lines. It also increased caspase 3. The solvent which contains ethyl acetate show the maximum cytotoxicity activity. 14-deoxyandrographolide, andrographolide, neoandrographolide, deoxyandrographiside are present in ethyl acetate fraction (46). *Andrographis paniculata* also inhibited esophageal cancer. The water extract stops the TM4SF3 gene expression. It also inhibited the EC-109, KYSE0520. The water extract inhibited the pre-step of metastasis without doing cell toxicity (56,6,7,8,28). **Figure-4** shows the activity of andrographolide in cancer cells.

Immunomodulatory Activity

The methanolic extract of *Andrographis paniculata*'s aerial parts and dichloromethane fraction of chemical constituents like 14-deoxy-11-didehydroandrographolide,12-didehydroandrographolide, andrographolide, 14-deoxyandrographolide are isolated from the plant. The extract at a concentration of 1uM induced the human peripheral blood lymphocytes i.e HPBL proliferation by fourteen, fifteen, and seven percent.

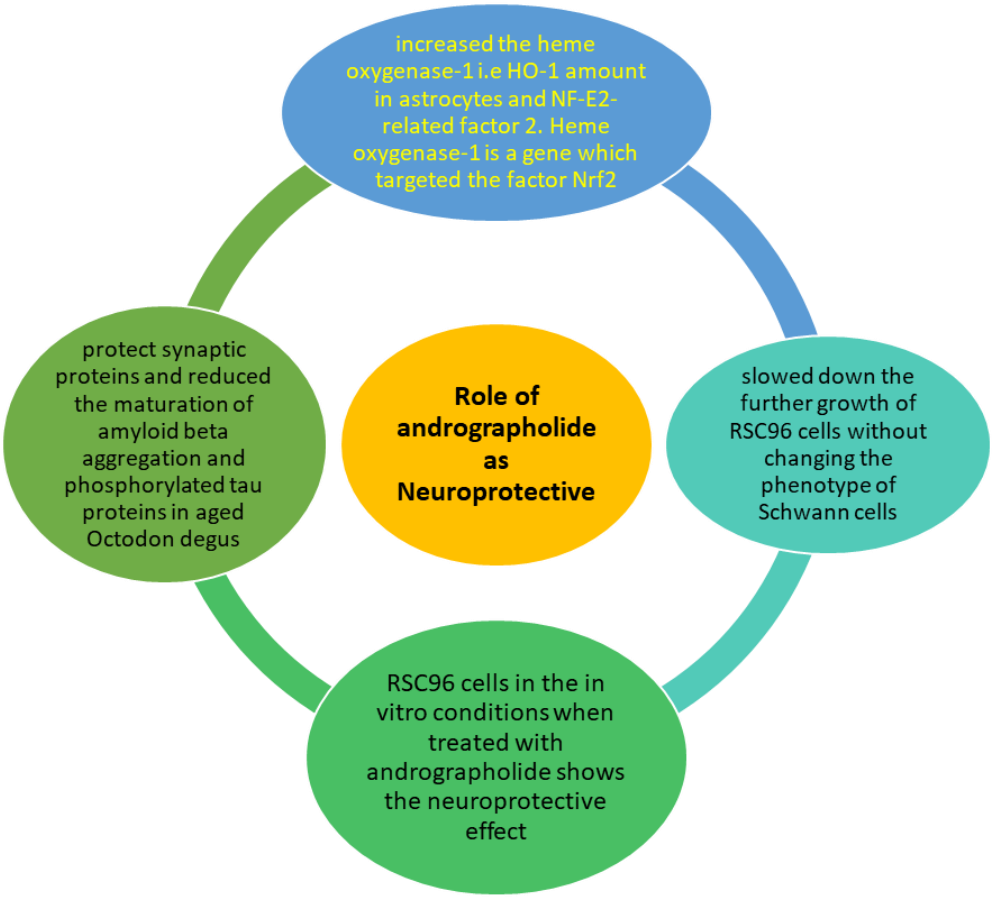


Fig 3. Role of andrographolide as Neuroprotective.

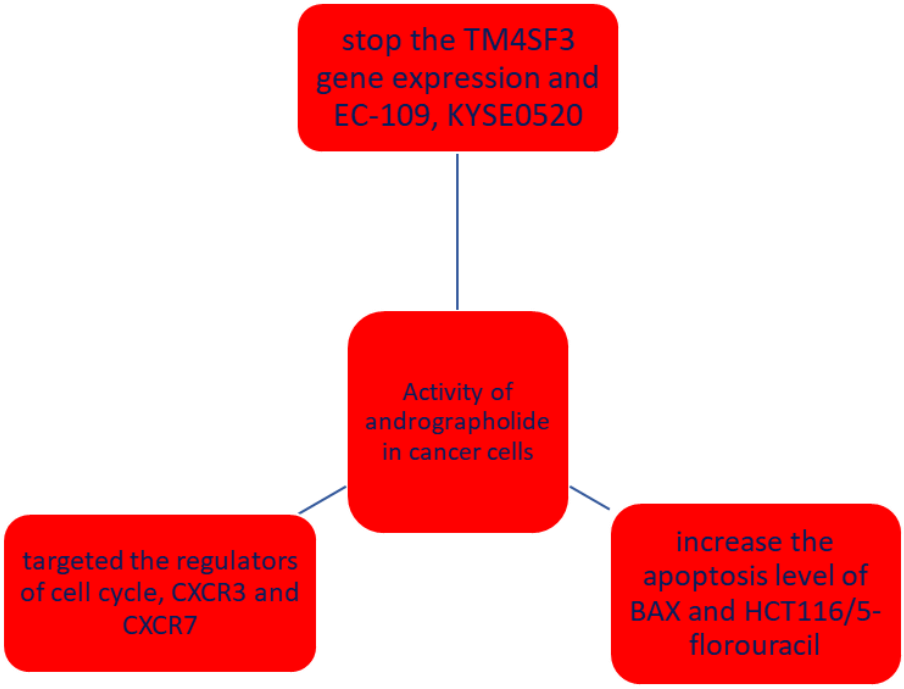


Fig 4. Activity of andrographolide in cancer cells.

The 14-deoxy-11-didehydroandrographolide,12-didehydroandrographolide, 14-deoxyandrographolide increase the induction of IL-2 in human peripheral blood lymphocytes i.e HPBL. Andrographolide increased the IL-2 induction and it can also cause toxicity in cells of HPBLs at higher concentrations (56).

Antimicrobial Activity

The aqueous extract of *Andrographis paniculata*, arabinogalactan proteins, and andrographolide from *Andrographis paniculata* showed antimicrobial activity. They showed antimicrobial activity against *Candida albicans*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus subtilis,* and *Staphylococcus aureus*. The aqueous extract of *Andrographis paniculata* showed the same or synergistic effect as arabinogalactan proteins and andrographolide showed (43). In the disc diffusion assay, the methanolic extract of leaves of *Andrographis paniculata* with the concentration of 5 mg/disc showed antimicrobial activity against Staphylococcus aureus and Bacillus cereus. The methanolic extract of leaves of *Andrographis paniculata* contains 73.40 mg/g of andrographolide in HPLC estimation which are responsible for showing antimicrobial activity. In the cup plate agar diffusion assay, the methanolic extract of leaves of *Andrographis paniculata* showed antibacterial activity. The extract showed antibacterial activity against the *Staphylococcus aureus*, *Micrococcus luteus*, *Proteus mirabilis, Staphylococcus pyogenes, Pseudomonas aeruginosa*. The *Pseudomonas aeruginosa* showed the lowest activity and *Staphylococcus aureus* showed the highest activity at concentration 1 mg/ml1. A bioautography study was also done in which MeOH extract was used to spot on bioautogram against the indicator organisms Pseudomonas and Staphylococcus aureus. This study helps in the isolation and identification of 14-deoxyandrographolide and 3-O-beta-D-glucosyl-14-deoxyandrographolide. Both compounds are antibacterial. Both compounds are NMR spectra based. The hydro ethanolic extract of *Andrographis paniculata* also showed antimicrobial as well as antibiofilm activity against Salmonella typhimurium. Salmonella typhimurium is a type of pathogen which is developed from food. The extract agitates and damages the membrane of Salmonella typhimurium (19). Silver nanoparticles of *Andrographis paniculata* showed the highest antibacterial activity against Gram-positive *Enterococcus faecalis*. Silver nanoparticles and Gram-positive *Enterococcus faecalis* showed a large gap in values of zeta potential. The charge on the surface of cells kills the cells (26). The 14-deoxy-11-didehydroandrographolide,12-didehydroandrographolide decreased the H1N1 influenza A virus and H5N1 influenza A virus in the mice. 3,19-isopropylideneandrographolide from the diterpenoid lactone category stopped the infection of herpes simplex virus type-1 (19).

Hepatoprotective

Chen et al. in 2000 had demonstrated that the *Andrographis paniculata* ethanolic extract and andrographolide therapeutically maintained the amount of P-glycoprotein, UGT i.e uridine diphosphate glucuronosyl transferases, cytochrome P450 isoenzymes activity, and GST i.e glutathione S-transferases in the liver of the rat. The rats were also used to study the effect of andrographolide and ethanolic extract on the pharmacokinetically activity of tolbutamide. Andrographolide and the ethanolic extract were also studied for the hypoglycaemic side effect produced by tolbutamide in the mice which was obese by giving them a high amount of fat diet. The concentration of the dose of andrographolide was 50 mg/kg per day and 2 g/kg per day methanolic extract by the route of intragastric for five days. Both doses were given before the administration of the tolbutamide dose i.e 20 mg/kg. The andrographolide and ethanolic extract decreased the amount of tolbutamide by inducing enzymes that metabolize the drug without damaging the hypoglycaemic activity of tolbutamide. Andrographolide helps in protecting the liver cells from cell death produced by H2O2 by inducing Nrf-2/HO-1 by the signaling of A2a receptors.

Analgesic activity

Lin FL et al. in 2009 had demonstrated that the extract of *Andrographis paniculata* and andrographolide showed analgesic activity (22). Ghosh et al. in 1981 had demonstrated that the use of *Andrographis paniculata* by the route of oral in the concentration dose of 20-30 ml/kg showed the analgesic and anti-inflammatory activity (45).

Anti-Pyretic activity

Amarayan et al. in 2003 had demonstrated that the *Andrographis paniculata* when given with the *Glychrrizhia glabra, Eletherococcus senticosus* and *Schisandra chinesis* combination showed the therapeutic activity against the Mediterranean fever. The combination was in fixed and standardized dose by double-blind and a clinical trial among two groups of patients was done (3). Anbarasu et al. in 1999 had demonstrated that chikungunya fever can be treated by the chooranam of *Andrographis paniculata*. Mahadev et al. in 2000 has demonstrated that the andrographolide dose in a concentration of 300 mg/kg showed analgesic activity in mice which were suffered from wriggle

pain induced by acetic acid and Randall test. The andrographolide does not respond to any analgesic activity in the mice which was put on a hot plate. The rats were given brewers yeast to develop fever and raise the temperature and the antipyretic activity was demonstrated by administration of andrographolide dose at 100 mg/kg and 300 mg/kg by oral route. The antipyretic effect of andrographolide was produced after three hours. Andrographolide also showed anti-ulcer activity in aspirin-induced ulcers in rats (5).

Anti-diabetic activity

The ethanolic extract of *Andrographis paniculata* showed anti-diabetic activity in rats that were diabetic by the streptozotocin. The extract also reduced the level of glucose in the blood and the level of triglyceride by 49.8 percent (54) in the streptozotocin-induced diabetic rats (57). Borhanuddin et al. in 1994 had reported the hypoglycaemic activity of hydro extract (dose concentration is 10 mg/kg) of *Andrographis paniculata*. The extract was given to the hyperglycaemic rabbits whose hyperglycaemic level is induced by 2 mg/kg glucose by the oral route (9). Koteswara Rao in 2006 had demonstrated that the chloroform extract of roots of *Andrographis paniculata* showed antihyperglycemic activity. The extract was given to the diabetic rats whose diabetes was induced by alloxan. Nugroho et al. in 2000 had demonstrated that the *Andrographis paniculata* and andrographolide showed antihyperlipidemic and antidiabetic activity in the rats which were fed a fatty diet. To increase the body weight, cholesterol in the blood, glucose in the blood, triglycerides, and low-density lipoproteins the rats were fed with high fructose-containing fat for fifty-five days regularly. The high fructose-containing fat diet contains fifteen percent lard, five percent egg yolk, thirty-six percent fructose. The study demonstrated that the andrographolide can lower the glucose level in plasma through utilizing the glucose in insulin lack diabetic rats (54). The combination of *Andrographis paniculata* and *Momordica charantia* showed an antidiabetic effect in diabetic rats whose diabetes was induced by giving alloxan (44).

Anti-platelet activity

Thisoda et al. in 2006 had demonstrated that the extract of *Andrographis paniculata* contains many anti platelets chemical components which have a vital role in the anti-platelet activity. The chemical components like andrographolide, 14-deoxy-11-didehydroandrographolide, 14-deoxy-12-didehydroandrographolide helped in the inhibition of platelets aggregation induced by thrombin in the time versus concentration graph. The extract of *Andrographis paniculata* and its other chemical constituents induced Enos-NO/cyclic-GMP pathway by reducing PLCgama2-PKC and PI3 Kinase/Akt-MAOKs (24) and reducing the factor that activates platelet (25). Amroyan et al. in 1999 had demonstrated that the platelet aggregation induced by PAF was inhibited by the andrographolide in a dose-dependent manner i.e 5uM. Andrographolide exhibited activity on the cardiovascular system and antithrombotic activity. The mechanism of action of andrographolide differs from NSAIDS i.e non-steroidal anti-inflammatory drugs (4).

Anti-bacterial activities

Ahmed et al. in 2012 had demonstrated that the methanolic extract of the whole part of the plant was used to isolate the compound named 3-O-beta-Dglycosyl-14-deoxyandrographolide by the bioassay-guided isolation method. The 3-O-beta-Dglycosyl-14-deoxyandrographolide exhibited antibacterial activity (1,47,49). There is a total of nine strains of bacteria on which *Andrographis paniculata* showed anti-bacterial activity. The strains are *Escherichia coli, Staphylococcus aureus, Salmonella typhimurium, Shigella sonnei, Bordetella pertussis, Legionella pneumophila, Staphylococcus pyogenes, Staphylococcus pneumonia, Pseudomonas aeruginosa* (18,53).

Toxicity studies

The toxicity of andrographolide and other members of the *Andrographis paniculata* family of chemicals is extremely low. Mice given oral extracts of *Andrographis paniculata* (10 g/kg body weight) once a day for seven days were able to survive and none perished. This large dose resulted in a decrease in activity and an overall feeling of drowsiness. These animals' hearts, kidneys, livers, and spleens were all found to be normal. There was no effect on growth, appetite, or stool production when mice were administered 500 mg/kg of *Andrographis paniculata* daily for 10 days. The animals were lively, and total blood counts came back normal. There were no adverse cardiovascular reactions in rabbits administered intravenous andrographolide (10 mg/kg). Heart, liver, kidney, and spleen enzyme testing were performed was normal. When handled correctly, andrographolides are naturally occurring chemicals with low toxicity. Allergic responses have been linked to the use of *Andrographis paniculata*, ranging from small skin rashes to more serious anaphylaxis, which could be a problem at high doses. It's unclear if these reactions are caused by *Andrographis paniculata* or by other substances in herbal preparations (60,61).

Conclusions

After analyzing all of *Andrographis paniculata* 's ayurvedic and modern scientific characteristics, this medicinal herb can be recommended to the general public as a safe and important source of healthcare. It has been found that *Andrographis paniculata* (Kalmegh) is a therapeutically beneficial plant for infections, fever, respiratory diseases, snake bites, worm infections, and a variety of other ailments. Its active phytochemical components have been linked to a variety of medicinal benefits. According to the study, Kalmegh has anti-inflammatory, anti-diabetic, anti-cancerous, anti-venom, antipyretic, hepatoprotective, and other pharmacological properties. This plant can also be used to generate herbal formulations for the treatment of a variety of ailments due to the presence of various bioactive components and a low toxicity profile. The plant is widely cultivated in many parts of the world, and its prominence as a medicinal plant is developing rapidly as more and more evidence of its numerous therapeutic applications emerges. The present article reviews the pharmacological activities of Kalmegh. So, more research work should be done for the safe and effective use of *Andrographis paniculata* crude drug. There are many other species of Andrographis plant on which pharmacological activities have not been done. So, there is a need for more work on other species and marketed formulations.

Contribution of authors

The author has done exhaustive literature survey from google scholar, pubmed, shodhganga etc, and various search engines to put best knowledge.

Acknowledgments

The author wants to thank the Department of Pharmaceutical sciences, Maharshi Dayanand University, Rohtak.

Conflict of interest

There is no conflict of interest by the author.

References

1. Ahmed QU, Samah OA, Sule A. *Andrographis paniculata* (Burm. f) Wall. ex Ness: a potent antibacterial plant. Antimicrobial Agents. 2012 Sep 12:345-60. 10.5772/34420.
2. Al-Henhena N, Ying RP, Ismail S, Najm W, Khalifa SA, El-Seedi H, Abdulla MA. Chemopreventive efficacy of *Andrographis paniculata* on azoxymethane-induced aberrant colon crypt foci in vivo. PloS one. 2014 Nov 12;9(11):e111118. https://doi.org/10.1371/journal.pone.0111118
3. Amaryan G, Astvatsatryan V, Gabrielyan E, Panossian A, Panosyan V, Wikman G. Double-blind, placebo-controlled, randomized, pilot clinical trial of ImmunoGuard®–a standardized fixed combination of *Andrographis paniculata* Nees, with Eleutherococcus senticosus Maxim, Schizandra chinensis Bail. and Glycyrrhiza glabra L. extracts in patients with Familial Mediterranean Fever. Phytomedicine. 2003 Jan 1;10(4):271-85. https://doi.org/10.1078/094471103322004767
4. Amroyan E, Gabrielian E, Panossian A, Wikman G, Wagner H. Inhibitory effect of andrographolide from *Andrographis paniculata* on PAF-induced platelet aggregation. Phytomedicine. 1999 Mar 1;6(1):27-31. https://doi.org/10.1016/S0944-7113(99)80031-2
5. Anbarasu K, Manisenthil KK, Ramachandran S. Antipyretic, anti-inflammatory and analgesic properties of nilavembu kudineer choornam: a classical preparation used in the treatment of chikungunya fever. Asian Pacific journal of tropical medicine. 2011 Oct 1;4(10):819-23. https://doi.org/10.1016/S1995-7645(11)60201-0
6. Anbarasu K, Manisenthil KK, Ramachandran S. Antipyretic, anti-inflammatory and analgesic properties of nilavembu kudineer choornam: a classical preparation used in the treatment of chikungunya fever. Asian Pacific journal of tropical medicine. 2011 Oct 1;4(10):819-23. https://doi.org/10.1016/S1995-7645(11)60201-0
7. Bailey AM, Mahapatra S, Brennan PJ, Crick DC. Identification, cloning, purification, and enzymatic characterization of Mycobacterium tuberculosis 1-deoxy-D-xylulose 5-phosphate synthase. Glycobiology. 2002 Jan 1;12(12):813-20. https://doi.org/10.1093/glycob/cwf100
8. Banerjee M, Chattopadhyay S, Choudhuri T, Bera R, Kumar S, Chakraborty B, Mukherjee SK. Cytotoxicity and cell cycle arrest induced by andrographolide lead to programmed cell death of MDA-MB-231 breast cancer cell line. Journal of biomedical science. 2016 Dec;23(1):1-7. https://doi.org/10.1186/s12929-016-0257-0
9. Borhanuddin M, Shamsuzzoha M, Hussain AH. Hypoglycaemic effects of *Andrographis paniculata* Nees on non-diabetic rabbits.

Bangladesh Medical Research Council Bulletin. 1994 Apr 1;20(1):24-6.
10. C.Y. Zhang, B.K.H. Tan. (1997). Comparison of pharmacological effect of four andrographolides. Chinese Pharm Bull. 1982; 17:195-198. https://doi.org/10.1016/S0378-8741(97)01509-2.
11. Cai W, Chen S, Li Y, Zhang A, Zhou H, Chen H, Jin M. 14-Deoxy-11, 12-didehydroandrographolide attenuates excessive inflammatory responses and protects mice lethally challenged with highly pathogenic A (H5N1) influenza viruses. Antiviral research. 2016 Sep 1;133:95-105. https://doi.org/10.1016/j.antiviral.2016.07.020
12. Chao WW, Kuo YH, Lin BF. Anti-inflammatory activity of new compounds from *Andrographis paniculata* by NF-κB transactivation inhibition. Journal of agricultural and food chemistry. 2010 Feb 24;58(4):2505-12. https://doi.org/10.1021/jf903629j
13. Chaudhary K, Parihar S, Sharma D. A Critical Review on Nanoscience Advancement: In Treatment of Viral Infection. Journal of Drug Delivery and Therapeutics. 2021 Nov 15;11(6):225-37.
14. Dai Y, Chen SR, 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 Jun 27;59(sup1):S17-29. https://doi.org/10.1080/10408398.2018.1501657
15. Daw khin, win myint. (1997). Government of the union of myanmar.ministry of forestry. Forest department. Forest research institute. Studies on the macroscopic and microscopic characters of some leaves used in indigenous medicine of myanmar.11:95-96. http://www.efi.int/portal/projects/flegt.
16. Gao H, Wang J. Andrographolide inhibits multiple myeloma cells by inhibiting the TLR4/NF-κB signaling pathway. Molecular medicine reports. 2016 Feb 1;13(2):1827-32. https://doi.org/10.3892/mmr.2015.4703
17. Jain, P.K., Ravichandran, V., Jain, P., & Agrawal, R. (2010). High-performance thin layer chromatography method for estimation of andrographolide in herbal extract and polyherbal formulations. Journal of Saudi Chemical Society, 14, 383- 389.
18. Jiang X, Yu P, Jiang J, Zhang Z, Wang Z, Yang Z, Tian Z, Wright SC, Larrick JW, Wang Y. Synthesis and evaluation of antibacterial activities of andrographolide analogues. European journal of medicinal chemistry. 2009 Jul 1;44(7):2936-43. https://doi.org/10.1016/j.ejmech.2008.12.014
19. Kongyingyoes B, Priengprom T, Pientong C, Aromdee C, Suebsasana S, Ekalaksananan T. 3, 19-isopropylideneandrographolide suppresses early gene expression of drug-resistant and wild type herpes simplex viruses. Antiviral research. 2016 Aug 1;132:281-6. https://doi.org/10.1016/j.antiviral.2016.07.012
20. Kumar RA, Sridevi K, Kumar NV, Nanduri S, Rajagopal S. Anticancer and immunostimulatory compounds from *Andrographis paniculata*. Journal of ethnopharmacology. 2004 Jun 1;92(2-3):291-5. https://doi.org/10.1016/j.jep.2004.03.004
21. Lee YC, Lin HH, Hsu CH, Wang CJ, Chiang TA, Chen JH. Inhibitory effects of andrographolide on migration and invasion in human non-small cell lung cancer A549 cells via down-regulation of PI3K/Akt signaling pathway. European journal of pharmacology. 2010 Apr 25;632(1-3):23-32. https://doi.org/10.1016/j.ejphar.2010.01.009
22. Lin FL, Wu SJ, Lee SC, Ng LT. Antioxidant, antioedema and analgesic activities of *Andrographis paniculata* extracts and their active constituent andrographolide. Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives. 2009 Jul;23(7):958-64. https://doi.org/10.1002/ptr.2701
23. Liu C, Nadiminty N, Tummala R, Chun JY, Lou W, Zhu Y, Sun M, Evans CP, Zhou Q, Gao AC. Andrographolide targets androgen receptor pathway in castration-resistant prostate cancer. Genes & cancer. 2011 Feb;2(2):151-9.
24. Lu B, Sheng Y, Zhang J, Zheng Z, Ji L. The altered microRNA profile in andrographolide-induced inhibition of hepatoma tumor growth. Gene. 2016 Aug 22;588(2):124-33. https://doi.org/10.1016/j.gene.2016.05.012.
25. Lu WJ, Lee JJ, Chou DS, Jayakumar T, Fong TH, Hsiao G, Sheu JR. A novel role of andrographolide, an NF-kappa B inhibitor, on inhibition of platelet activation: the pivotal mechanisms of endothelial nitric oxide synthase/cyclic GMP. Journal of Molecular Medicine. 2011 Dec;89(12):1261-73.

https://doi.org/10.1007/s00109-011-0800-0
26. Mandal D, Dash SK, Das B, Chattopadhyay S, Ghosh T, Das D, Roy S. Bio-fabricated silver nanoparticles preferentially targets Gram positive depending on cell surface charge. Biomedicine & Pharmacotherapy. 2016 Oct 1;83:548-58. https://doi.org/10.1016/j.biopha.2016.07.011
27. Mir H, Kapur N, Singh R, Sonpavde G, Lillard Jr JW, Singh S. Andrographolide inhibits prostate cancer by targeting cell cycle regulators, CXCR3 and CXCR7 chemokine receptors. Cell Cycle. 2016 Mar 18;15(6):819-26. https://doi.org/10.1080/15384101.2016.1148836
28. Mishra SK, Tripathi S, Shukla A, Oh SH, Kim HM. Andrographolide and analogues in cancer prevention. Front Biosci (Elite Ed). 2015 Jan 1;7(5):255-66. https://doi.org/10.2741/E732
29. Nadiminty N, Lou W, Sun M, Chen J, Yue J, Kung HJ, Evans CP, Zhou Q, Gao AC. Aberrant activation of the androgen receptor by NF-κB2/p52 in prostate cancer cells. Cancer research. 2010 Apr 15;70(8):3309-19. https://doi.org/10.1158/0008-5472.CAN-09-3703
30. Parihar S, Sharma D. Cynodondactylon: A Review of Pharmacological Activities. Sch Acad J Pharm. 2021 Nov;11:183-9.
31. Parihar S, Sharma D. Navagraha (nine planets) plants: the traditional uses and the therapeutic potential of nine sacred plants of india that symbolises nine planets. IJRAR. 2021;8(4):96-108.
32. Parihar S, Sharma D. A brief overview on Asparagus racemous. IJRAR Dec. 2021;8(4):96-108.
33. Parihar S, Sharma D. A brief overview on Vitis Vinifera. Sch Acad J Pharm. 2021 Dec;12:231-9.
34. Parihar S, Sharma D. A Brief Overview on Crinum Latifolium. Phytochemistry. 2021;7(14):24.
35. Parihar, S., Chattarpal, Sarswati, Hooda, S., 2022. Moringa oleifera Extract- "A Miracle Tree". Sch Acad J Pharm, 11(1): 1-5.
36. Parihar, S., Chattarpal., Sharma, D. 2022. Literature review on the list of the plants used in the treatment of lung cancer. WJPPS. 11(1), 2025-2029.
37. Rafat A, Philip K, Muni S. Antioxidant potential and content of phenolic compounds in ethanolic extracts of selected parts of *Andrographis paniculata*. Journal of Medicinal Plants Research. 2010 Feb 4;4(3):197-202.
38. Rao NK. Anti-hyperglycemic and renal protective activities of *Andrographis paniculata* roots chloroform extract. (2006): 47-50.
39. Rivera DS, Lindsay C, Codocedo JF, Morel I, Pinto C, Cisternas P, Bozinovic F, Inestrosa NC. Andrographolide recovers cognitive impairment in a natural model of Alzheimer's disease (Octodon degus). Neurobiology of aging. 2016 Oct 1;46:204-20. https://doi.org/10.1016/j.neurobiolaging.2016.06.021
40. Archit R, Mythili S, Sathiavelu A. Sangeetha1. Int. J. Drug Dev. & Res. 2014 Jan;6(1):0975-9344.
41. Shen YC, Chen CF, Chiou WF. Andrographolide prevents oxygen radical production by human neutrophils: possible mechanism (s) involved in its anti-inflammatory effect. British journal of pharmacology. 2002 Jan;135(2):399-406. https://doi.org/10.1038/sj.bjp.0704493
42. Shi MD, Lin HH, Lee YC, Chao JK, Lin RA, Chen JH. Inhibition of cell-cycle progression in human colorectal carcinoma Lovo cells by andrographolide. Chemico-biological interactions. 2008 Aug 11;174(3):201-10.
43. Singha PK, Roy S, Dey S. Antimicrobial activity of *Andrographis paniculata*. Fitoterapia. 2003 Dec 1;74(7-8):692-4. https://doi.org/10.1016/s0367-326x(03)00159-x
44. Subramanian R, Asmawi MZ, Sadikun A. Effect of andrographolide and ethanol extract of *Andrographis paniculata* on liver glycolytic, gluconeogenic, and lipogenic enzymes in a type 2 diabetic rat model. Pharmaceutical Biology. 2008 Jan 1;46(10-11):772-80.
45. Suebsasana S, Pongnaratorn P, Sattayasai J, Arkaravichien T, Tiamkao S, Aromdee C. Analgesic, antipyretic, anti-inflammatory and toxic effects of andrographolide derivatives in experimental animals. Archives of pharmacal research. 2009 Sep;32(9):1191-200. https://doi.org/10.1007/s12272-009- 1902-x
46. Suzuki R, Matsushima Y, Okudaira N, Sakagami H, Shirataki Y. Cytotoxic components against human oral squamous cell carcinoma isolated from *Andrographis paniculata*. Anticancer research. 2016 Nov 1;36(11):5931-5. https://doi.org/10.21873/anticanres.11180
47. Tanwar A, Chawla R, Chakotiya AS, Thakur P, Goel R, Basu M, Arora R, Khan HA. Effect of Holarrhena antidysentrica (Ha) and *Andrographis paniculata* (Ap) on the biofilm formation and cell membrane integrity of

opportunistic pathogen Salmonella typhimurium. Microbial pathogenesis. 2016 Dec 1;101:76-82. https://doi.org/10.1016/j.micpath.2016.11.001

48. Telrandhe UB, Lokhande RR, Lodhe VN, Kosalge SB, Parihar S, Sharma D. Review on Herbal Drugs used in Dental Care Management. Asian Journal of Pharmaceutical Research and Development. 2021;9(6):71-9.
49. V. Soumya, Y. Indira Muzib, P. Venkatesh. (2014) GC-MS Characterization, in vitro Antioxidant and Antimicrobial Activity of Newly Isolated Oil from Edible Wild Bamboo Rice (Bambusa bambos). Journal of Biologically Active Products from Nature 4:3, pages 209-215
50. Wang W, Guo W, Li L, Fu Z, Liu W, Gao J, Shu Y, Xu Q, Sun Y, Gu Y. Andrographolide reversed 5-FU resistance in human colorectal cancer by elevating BAX expression. Biochemical pharmacology. 2016 Dec 1;121:8-17. https://doi.org/10.1016/j.bcp.2016.09.024
51. Wong SY, Tan MG, Wong PT, Herr DR, Lai MK. Andrographolide induces Nrf2 and heme oxygenase 1 in astrocytes by activating p38 MAPK and ERK. Journal of neuroinflammation. 2016 Dec;13(1):1-2. https://doi.org/10.1186/s12974-016-0723-3
52. Xu F, Wu H, Zhang K, Lv P, Zheng L, Zhao J. Pro neurogenic effects of andrographolide on RSC96 Schwann cells in vitro. Molecular medicine reports. 2016 Oct 1;14(4):3573-80. https://doi.org/10.3892/mmr.2016.5717
53. Sareer O, Ahmad S, Umar S. *Andrographis paniculata*: a critical appraisal of extraction, isolation and quantification of andrographolide and other active constituents. Natural product research. 2014 Dec 2;28(23):2081-101.
54. Yu BC, Chen WC, Cheng JT. Antihyperglycemic effect of andrographolide in streptozotocin-induced diabetic rats. Planta medica. 2003 Dec;69(12):1075-9. https://doi.org/10.1055/s-2003-45185
55. Yuan H, Sun B, Gao F, Lan M. Synergistic anticancer effects of andrographolide and paclitaxel against A549 NSCLC cells. Pharmaceutical biology. 2016 Nov 1;54(11):2629-35. https://doi.org/10.1080/13880209.2016.1176056
56. Yue GG, Lee JK, Li L, Chan KM, Wong EC, Chan JY, Fung KP, Lui VW, Chiu PW, Bik-San Lau C. *Andrographis paniculata* elicits anti-invasion activities by suppressing TM4SF3 gene expression and by anoikis-sensitization in esophageal cancer cells. American journal of cancer research. 2015;5(12):3570.
57. Zhang XF, Tan BH. Anti-diabetic property of ethanolic extract of *Andrographis paniculata* in streptozotocin-diabetic rats. Acta Pharmacologica Sinica. 2000 Dec 1;21(12):1157-64.
58. Zhou J, Ong CN, Hur GM, Shen HM. Inhibition of the JAK-STAT3 pathway by andrographolide enhances chemosensitivity of cancer cells to doxorubicin. Biochemical pharmacology. 2010 May 1;79(9):1242-50. https://doi.org/10.1016/j.bcp.2009.12.014
59. Zou W, Xiao Z, Wen X, Luo J, Chen S, Cheng Z, Xiang D, Hu J, He J. The anti-inflammatory effect of *Andrographis paniculata* (Burm. f.) Nees on pelvic inflammatory disease in rats through down-regulation of the NF-κB pathway. BMC complementary and alternative medicine. 2016 Dec;16(1):1-7. https://doi.org/10.1186/s12906-016-1466-5S
60. Mishra SK, Sangwan NS, Sangwan RS. Phcog rev.: Plant review *Andrographis paniculata* (Kalmegh): A review. Pharmacognosy Reviews. 2007 Jul;1(2):283-98.
61. Okhuarobo A, Falodun JE, Erharuyi O, Imieje V, Falodun A, Langer P. Harnessing the medicinal properties of *Andrographis paniculata* for diseases and beyond: a review of its phytochemistry and pharmacology. Asian Pacific journal of tropical disease. 2014 Jun 1;4(3):213-22.
62. Grover M. Green Chiryata (Andrographis paniculata): A potential blood purifier. International research journal of pharmacy and medical sciences. 2021; 4(5).