

# An Overview on Chemical Aspects and Potential Health Benefits of Andrographolide

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# **Abstract**

Andrographolide is a main chemical constituent of Andrographis paniculata that having medicinal and pharmacological properties for various diseases. In this present work, we study their multiple pharmacological properties - antimicrobial, anticancer, antifertility, antiinflammatory and antidiabetic activities. Andrographolide is an intriguing pharmacophore that has potential to be developed as a chemotherapeutic drug for the treatment of cancer. This suggests, it has anticancer and immunomodulatory properties. In order to understand the Andrographis paniculata plant as a multifunctional medicinal agent, we have investigated the several aspects of the plant and collated its extensive pharmacological properties with their applications in this review. The plant is widely cultivated in many parts of the world, and as more and more evidence of its numerous therapeutic applications suggesting the plant has dominant significance as a medicinal plant. Further, Andrographolide is an extremely bitter substance, so this is referred the "King of Bitters". Moreover, leaves and roots of Andrographis paniculata contain a labdane diterpenoid called andrographolide, which has anti-HIV, anti-inflammatory, and anti-cancer activities. It performs functions as a metabolite, analgesic, anti-HIV, and antineoplastic medication. It is a labdane diterpenoid, a labdane alcohol, a primary alcohol, a secondary alcohol, a carbocyclic molecule, and a gammalactone.

Keywords: Andrographis paniculata, andrographolide, neoandrographolide, hepatoprotective, anticancer, antitumor, anti-inflammatory, medicinal plant.

# 1. Introduction

The annual herb Andrographis paniculata is a member of the Acanthaceae family. The bioactive compound andrographolide is typically regarded as being vital to the plant A. paniculata. It has drawn interest from the scientific and medical communities for its therapeutic properties, which have been well known since ancient times. This review provides an overview of the molecule andrographolide molecular, clinical, and in vitro studies as well as its mode of action. When it mixed with other boosting substances, andrographolide provides a number of health advantages. Andrographolide has demonstrated its medicinal potential through indirectly interacting with small molecules and various enzymes, as well as by directly influencing genes. The pharmacological activity of andrographolide and its analogues is compiled and consolidated in this review, which also identifies the gaps that have prevented its adoption in medicinal research. [1]

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AP is an annual herbaceous plant that grows upright to a height of 30 to 110 cm in wet, and shaded areas. Its stem is abruptly quadrangular, heavily branched, and delicate in texture. Simple, opposite, lanceolate, glabrous leaves with a sharp, entire, or slightly undulating edge. Upper leaves are frequently bractiform and have a short petiole. The plant's inflorescence is described as plain, terminal, and axillary in panicle, measuring 10–30 mm long; the bract is tiny; and the pedicel is short. The flowers have the following botanical characteristics: a 5-particle, small, linear calyx; a narrow, about 6 mm long corolla tube; a limb longer than the tube, bilabiate; an upper lip that is broadly cuneate, 3-lobed, and white with violet markings; two stamens that are inserted in the throat and protrude far; and an anther.

Plant morphology: A. paniculata is an annual herb with several branches that is upright and has an exceptionally bitter flavour. It has glabrous leaves, grows to a height of 30 to 110 cm in wet, shady areas, and produces white flowers with rose-purple dots on the petals. The stem is dark green, 0.4-1.0 m tall, and 2–6 mm in diameter. Leaves are glabrous, up to 8.0 cm long and 2.6 cm wide, lanceolate, and pinnate; flowers are small and solitary, with hairy corollas in laxly spreading axillary and terminal racemes or icles; capsules are linear-oblong, acute at both ends, and measure 1.9-0.3 cm; seeds are numerous, subquadrate, and yellowish brown. The plant's capsule is upright, linear-oblong, compressed, longitudinally grooved on broad sides, sharp at both ends, and thinly glandular-haired. It is 1-2 cm long and 2-5 mm wide. Seeds are sub quadrate and very tiny. [2-6] The Andrographis paniculata plant produces andrographolide, a labdane diterpenoid with a wide range of medicinal uses, including anti-inflammatory and anti-platelet aggregation effects as well as putative antineoplastic characteristics. There are numerous suggested mechanisms of action for andrographolide because it has a variety of therapeutic effects.

#### 2. Authoritative/ Taxonomical Classification

The kingdom of plants: Plantae

The subkingdom: Tracheobionta, of vascular plants
Super division: Spermatophyta, of seed plants

Group: Angiosperms Class: Dicotyledonae Subclass: Gamopetalae, Series: Bicarpellatae Order: Personales Tribe: Justicieae Family: Acanthaceae Genus: Andrographis Species: paniculata





Fig. No. 1 Andrographis paniculata plant and its flower part

#### **Structure of Andrographolide**

IUPAC name 3-[2-[Decahydro-6-hydroxy-5-(hydroxymethyl)-5,8a-dimethyl-2-methylene-1-napthalenyl]ethylidene]dihydro-4-hydroxy-2(3H)-furanone

#### 3. Pharmacological Aspects of Andrographolide:

Andrographis paniculata (Burn.f) Nees (family Acanthaceae) is a well-known medicinal plant in traditional Asian medicine that has been used for ages to treat infectious disorders and the fevers that cure them. It is also well-known as a popular detoxifier, a carminative, and a tonic for liver and digestive issues [7]. It is commonly cultivated throughout Southeast Asia, including Malaysia, despite being indigenous to India and Sri Lanka. A. paniculata's pharmacological activities, including its anti-inflammatory, anticancer, immunomodulation, anti-HIV, antibacterial, antispasmodic, antidiabetic, anticarcinogenic, antipyretic, hepatoprotective, anti-infective, and antioxidant effects, have been the subject of numerous scientific reports [8-11]. Kan Jang, a Traditional Chinese Medicine (TCM) formula, is promoted as herbal treatment for respiratory issues and the common cold in China. Among the several uses for ethno medicine.

Andrographis paniculata has been extensively studied, particularly with much focus "AP's" pharmacological composition, safety, efficacy, and mechanisms of action during the second half of the 20th century [12-16]

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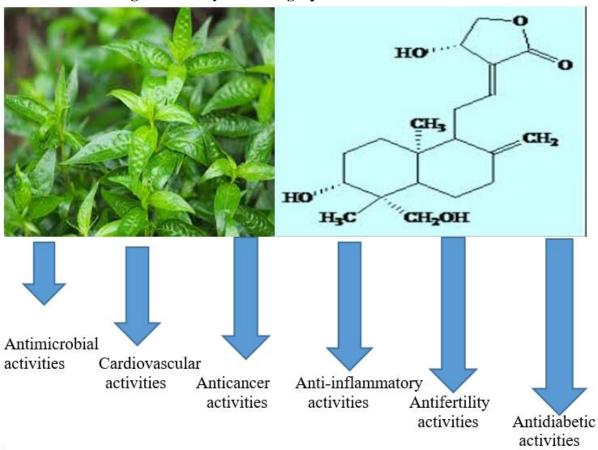
- Abortifacient (may cause pregnancy to end; although Ayurvedic tradition permits it to be used for a brief period during pregnancy, all women are urged to avoid its usage as a precaution).
   Andrographis is remarkably non-toxic in practically all other aspects.
   (hot: in this instance, mildly skin-ruffling)
- Analgesic (pain reliever) decreases inflammation and capillary exudation; this activity is likely mediated in part by adrenal function.
- Antibacterial (reduces bacterial activity; andrographis appears to have poor direct antibacterial action, but it has a notably favourable effect in lowering diarrhoea and bacterial illness symptoms.)
- Antiperiodic (fights off periodic/episodic illnesses like malaria)
- Antipyretic (fever reducer; used to treat both human and animal fever brought on by poisons or various illnesses)
- Thrombolytic (blood clot preventative)
- Viricides (inhibits viral activity) Cancer-fighting (fights, even kills, cancer cells)
- Heart-healthy (protects heart muscles)
- Coughing (alters the properties and flow of bile)
- Depurative (purges and cleanses the body, especially the blood)
- The digestive (promotes digestion)
- Expectorant (helps the respiratory system expel mucus)
- Hepatoprotective (guards the gallbladder and liver)
- Low blood sugar (blood sugar reducer)
- Immune Enhancement (boosts CD4 + and T lymphocyte numbers, suppresses HIV-1 replication, and promotes white cell phagocytosis)
- Diuretic (aids bowel elimination)
- Sedative (calming plant; less effective than commonly used herbal sedatives as valerian root, hops, skullcap, etc.)
- Antithrombotic (blood clot buster)

# 4. Antioxidant Properties of Andrographolide:

The antioxidant properties of A. paniculata and its components have been documented in numerous research [17-18]. According to Verma and Vinayak the aqueous extract of A. paniculata considerably increased the activities of antioxidant defence enzymes such glutathione -S-transferase, catalase, and superoxide dismutase while lowering glutathione level [19]. Andrographolide contributes to antioxidant defences [20-21]. It acts directly by neutralizing free radicals. Also, it interferes indirectly by protecting mitochondrial integrity, inhibiting pro-oxidant enzymes, and/or activating antioxidant enzymes. Antioxidants are just one of the many active components found in medicinal herbs. The use of natural antioxidants in the treatment of numerous diseases brought on by oxidative stress is of interest. Additionally, Andrographis paniculata has a long history of usage in Asian traditional medicine. Numerous studies have demonstrated that andrographolide, the primary bioactive component, has protective benefits against oxidative stress, particularly through Nrf2

activation. This review aimed to compile a wide range of papers concentrating on the antioxidant activity of andrographolide in order to understand the many processes involved. There are a number of possible processes that could account for andrographolide's antioxidant action. Both direct and indirect mechanisms [22] are possible. By defending mitochondria or by inhibiting particular ROS-producing enzymes, andrographolide can stop the generation of free radicals. It may also become active.

# 5. Pharmacological Activity of Andrographolide:



Since ancient times, South East Asia has employed andrographolide, the main labdane diterpene component of Andrographis paniculata (family Acanthaceae), extensively in traditional medicine. There is evidence that the plant's extracts and ingredients have a variety of biological properties of therapeutic value, including hepatoprotective, antimalarial, antibacterial, anti-inflammatory, antithrombotic, immunological stimulant, and anticancer properties. The literature contains reports on the synthesis of andrographolide derivatives for altering biological functions.

#### 6. Study about Antimicrobial Activities:

Antimicrobial medications have had a profound impact on humanity's fate as well as how infections are treated. Because of significant advancements in antimicrobial treatment, it has been speculated that infectious diseases may soon become extinct. In actuality, though, newly and emerging infectious illnesses have shown that infections are responding. Infections with drug-resistant organisms pose a pressing but difficult to understand challenge in clinical practise. If an inappropriate antimicrobial agent is chosen over the management of a drug-resistant microbial illness, the therapy may not be effective and may even worsen the

prognosis. It has been shown that A. paniculata and andrographolide showed strong antibacterial action against a variety of microorganisms. [23]

# 7. Study about Cardiovascular Activities:

A. paniculata has shown to enhance the time it takes for blood to clot; as a result, pre- and postoperative applications of the extract of A. paniculata greatly reduce blood vessel constriction and the danger of blood vessels shutting later on following angioplasty procedures [24]. Animal models have been employed in a number of research to examine the effects of aqueous extracts and the active ingredients in A. paniculata, both prior to and during an experimental myocardial infarction. Due to the plant's ability to relax the smooth muscles in blood vessel walls and stop the blood vessels from constricting and limiting blood flow to the brain, heart, and other organs, an extract of the plant had antihypertensive effects [25].

### 8. Study about Anticancer Activities:

It is known that natural ingredients can be used as source for medicines that cure a variety of human conditions, including cancer. Many natural medications made from plants include vincristine, irinotecan, etoposide, and paclitaxel [26]. Despite the fact that many medications of natural origin have been discovered, it is still required to look for novel anticancer agents in order to produce drugs that are less toxic and more effective as well as to enhance their diversity and availability. When choosing plants to treat cancer, samples with pharmacological applications should be taken into consideration because many illnesses reflect disease states relevant to cancer or cancer-like symptoms [27]. Both KB (human epidermoid leukaemia) and P388 (lymphocytic leukaemia) cells were highly toxic to by andrographolide [28]. Andrographolide was one of the diterpenoid lactones that was isolated from the A. paniculata ethyl acetate fraction and demonstrated potent anticancer activity by inducing cell differentiation in mice myeloid leukaemia cells [29]. Leukaemia, breast cancer, lung cancer, and melanoma cells were among the cell lines that andrographolide was reported to inhibit [30]. Additionally, this substance inhibits the advancement of the cell cycle, which has considerable anticancer action against human colorectal carcinoma LoVo cells [31].

# 9. Study about Anti-Inflammatory Activities:

The annual herb Andrographis paniculata is a member of the Acanthaceae family. The bioactive compound andrographolide is typically regarded as being vital to the plant A. paniculata. It has drawn interest from the scientific and medical communities for its therapeutic properties, which have been well known since ancient times. This review provides an overview of the molecule andrographolide molecular, clinical, and in vitro studies as well as its mode of action. When mixed with other boosting substances, andrographolide provides a number of health advantages. Andrographolide has demonstrated its medicinal potential by directly influencing genes and indirectly interacting with small molecules and other enzymes.

# 10. Study about Antifertility Activities:

The antifertility effects of andrographolide are characterised by large increases in cholesterol, acid phosphatase, and alkaline phosphatase levels with the advent of fructose in the rat reproductive systems, combined with severe decreases in protein content. [32] Rats' blood progesterone levels in response to AP's powdered extract. However, after 4 weeks of andrographolide administration, mice's testosterone levels considerably increased with

mounting frequency. For up to 8 weeks, therapy with andrographolide (50 mg/kg) had no adverse effects on sperm quantity or motility. Additional research is required to confirm the dual effects of andrographolide and AP on both male and female sexual behaviours. It would be beneficial to uncover precise mechanisms through which AP and its active ingredients regulate fertility and have contraceptive effects. [33-38]

# 11. Study about Antidiabetic Activities:

Kalmegh's antidiabetic effective component is discovered in the aerial, leaves and fruits and whole plant sections. Andrographolide is the main active ingredient in Andrographis paniculata for diabetic complications. It is easily available in tribal region and its already used by villagers for antidiabetic. It is called "King of bitters". So that its definitely reduce sugar percentage in body.

# 12. Chemistry of Andrographolide:

Kalmegh's therapeutically effective component is discovered in the aerial sections. Andrographolide is the main active ingredient in Andrographis paniculata. [39] Diterpene lactone is a colourless, crystalline substance that tastes harsh. Investigation of Andrographis paniculata revealed that it is a rich source of non-bitter compounds such as neoandrographolide (C26H40O8), homoandrographolide (C22H32O9), andrographosterol (C23H38O), andrographone (C32H64O), andrographane (C40H82O), andrographosterin, andrograpanin, stigmesterol, and Andrographolide [C20H30O5] (also known as 3-[2-decahydro-6-hydroxy-5-(hydroxymethyl)-5,8-dimethyl-2-methylene-1-napthalenyl]dihydro-4-hydroxy 2(3H)-furanone) is a colourless, crystalline bicyclic diterpenoid lactone that is found throughout the entire plant, but is most abundant in the leaves. Andrographolide appears to accumulate in organs throughout the viscera when taken orally.

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