

Pharmacological and Clinical Effects of *Andrographis paniculata*

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ABSTRACT

Andrographis paniculata is an herbaceous plant has been effectively used in traditional Asian medicines for centuries. The demand for the herbal drug treatment of various ailments is increasing day by day and plant drugs from the Ayurvedic system are being explored more in India as well as globally. The aerial part of the plant is used; it contains a large number of chemical components like diterpene, diterpenoid, glycosides, flavonoids as well as flavonoid glycosides. Andrographolide has been reported to have a wide range of biological activities, such as anti-inflammatory, anti-allergic, anti-platelet aggregations, hepatoprotective and anti-HIV. *A. paniculata* polysaccharides combined with andrographolide can be used in the recovery of diabetic nephropathy. In addition to these activities the ethanol and an aqueous extract of *A. paniculata* also decrease blood glucose levels in normal rats and streptozotocin diabetic rats. Andrographolide, reacts with several inter and intracellular constituents like a bipolar compound hence ensuing in many biological responses.

Key-words: *Andrographis paniculata*, Andrographolide, Anti-inflammatory, Biological activities

INTRODUCTION

A. paniculata is an herbaceous plant and it has been effectively used in traditional Asian medicines for centuries. Since the herbal drug treatment for various ailments is increasing and plant drugs from the Ayurvedic system are being explored more in India as well as globally. It is an annual plant of having 1-3 ft high. It is one of the most commonly used herbaceous plants in the traditional systems of Unani and Ayurvedic medicines. The biological activities from various clinical and preclinical studies have been summarized in this article [1]. It is also called Creat in English and is known as the "king of bitters".

It grows in hedgerows throughout the plains of India as

well as also cultivated in gardens [2,3]. It also grows in many other Asian countries. It is used as a traditional herbal medicine in several countries like China, Hong Kong, Philippines, Malaysia and Indonesia. It has been shown that the plant has "blood purifying" property; hence it can be used in diseases where the causes of disease are due to the blood abnormalities such as skin eruptions, boils, scabies and chronic undetermined fevers. For that purpose aerial part of the plant is used. It contains a large number of chemical components like diterpene, diterpenoid, glycosides, flavonoids as well as flavonoid glycosides. Report on the Controlled clinical trials shows that it's safe and effectively used for reducing symptoms of upper respiratory tract infections. Traditionally the plant was used as an infusion, decoction or as a powder either alone or in combination with other medicinal plants. It has been shown that in many controlled clinical trials, commercial preparations have tended to be standardized extracts of the whole plant. Many disease conditions commonly treated with *A. paniculata* in traditional medical systems is considered

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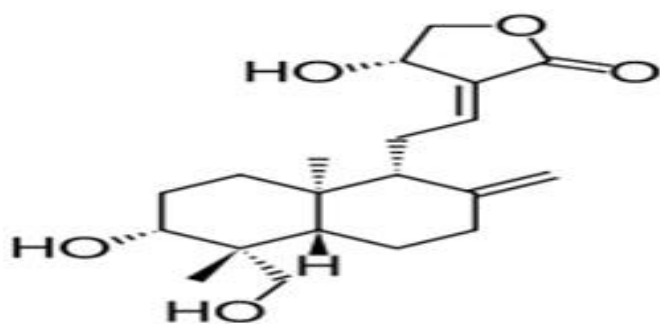
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[4]. This article aims to summarize the biological activities of few Indian medicinal plants.

Chemical Structure- Andrographolide is a major bioactive phytoconstituent which has been found in various parts of *A. paniculata*, mainly in the leaves. The chemical name of andrographolide is 3 α , 14, 15, 18-tetrahydroxy-5 β , 9 β H, 10 α -labda-8, 12-dien-16-oic acid γ -lactone and its molecular formula and weight are C₂₀H₃₀O₅ and 350.4 (C 68.54%, H 8.63%, and O 22.83%), respectively. The structure of andrographolide has been analyzed by using X-ray, 1H, 13 C-NMR, and ESI-MS [5-9]. Although andrographolide is not very soluble in water, it is soluble in acetone, chloroform, ether, and hot ethanol. It has been reported that the crystalline andrographolide was highly stable over a period of three months. It has been reported that a simple and rapid method was used for the isolating andrographolide from the leaf of *A. paniculata* [10].



Fig. 1: *Andrographis paniculata* plant



Andrographolide

Fig. 2: Chemical structure of Andrographolide

Biological activities of Andrographolide-

Andrographolide has been reported to have a wide range of biological activities, such as anti-inflammatory [11], antiallergic [12], antiplatelet aggregations [13,14], hepatoprotective [15] and anti-HIV [16]. In addition to these activities, ethanol and an aqueous extract of *A. paniculata* has the ability to decrease blood glucose levels in normal rats or streptozotocin diabetic rats. In biological systems, the andrographolide can interact with many inter- and intracellular constituents as a bipolar compound thus ensuing in many biological responses. A recent study demonstrated that *A. paniculata* polysaccharides combined with andrographolide, which can be used for the recovery of diabetic nephropathy [17].

Applications in Traditional medical systems- It has been reported that the plant has several medicinal properties like antibacterial, antifungal, antiviral, hypocholesterolemic, choleric, hypoglycaemic as well as adipogenic effects [18]. It has been used as aperient, anti-inflammatory, emollient, astringent, diuretic, emmenagogue, gastric and liver tonic, carminative, anti-helminthic and antipyretic in the Unani system of medicine. Since it has "blood purifying" properties, hence it has been recommended in cases of leprosy, gonorrhoea, scabies, boils, skin eruptions chronic and seasonal fevers. Juice or an infusion of fresh leaves is recommended for the infants to relieve griping, irregular bowel habits and loss of appetite. In the case of general debility, during convalescence after fevers and for dyspepsia associated with gaseous distension as well as in advanced stages of dysentery, leaves and root are also used [19,20]. In China, the herbal derivative obtained from the leaves or aerial parts of *A. paniculata* is known as Chuanxinlian, Yijianxi or Lanhelian. It was described as bitter and cold and having several properties like antipyretic, detoxicant, anti-inflammatory, and detumescent therefore it is thought to remove "pathogenic heat" from the blood. *A. paniculata* is used for the treatment of pharyngitis, diarrhea, dysentery and cough with thick sputum, carbuncle, sores, and snake bites. Various preparations and compound formulas of the herb have been used to treat infectious and non-infectious diseases, with significant effective rates reported for conditions such as epidemic encephalitis B, suppurative otitis media, neonatal subcutaneous annular ulcer, vaginitis, cervical erosion, pelvic inflammation, herpes

zoster, chickenpox, mumps, neurodermatitis, eczema and burns [21].

Modern application- Modern application of *A. paniculata* is for prevention as well as for the treatment of the common cold. It has also antithrombotic properties and recommending in cardiovascular disease [22]. Several Pharmacological and clinical studies indicating the potential for beneficial effects in diseases like cancer and HIV infections [23,24].

Pharmacological and clinical aspects of *Andrographis paniculata*

Hepatoprotective Effects- *A. paniculata* is used as a hepatoprotective and hepatostimulant agent in Indian systems of medicine [25]. *A. paniculata* is also an ingredient in several polyherbal preparations used as hepatoprotectants in India. One of which has been reported as efficacious in chronic hepatitis B virus infection. Very few studies on the effects of crude extracts of *A. paniculata* on liver function are available. Most studies for hepatic effects have been conducted on either andrographolide or other purportedly active principles. A comparative study on the effect of leaf extract of *Andrographis paniculata* has been conducted [26,27].

Antimicrobial and Antiparasitic Effects- In traditional systems of medicine *A. paniculata* has been extensively used for the treatment of a variety of infectious origin. Modern research has investigated it for activity against various bacteria, viruses, and parasites. Crude powder suspended in water was reported to be devoid of *in vitro* antibacterial activity against *Salmonella* sp., *Shigella* sp., *E. coli*, *Streptococci* sp., and *S. aureus* even at a concentration of 25 mg/mL crude powder [28]. It has been reported the previous study that shown the significant antibacterial activity of an aqueous extract and it has to be attributed by the combined effect of andrographolides and arabinogalactan proteins [29].

Antihyperglycemic and Hypoglycemic effects- Ethanol extract of *A. paniculata* increase the glucose secretion from the β cells of islets of langerhens and increase the surface uptake of glucose from the adipose tissue hence inhibit the glucose absorption. Aqueous extract of *A. paniculata* significantly prevents orally administered

glucose-induced hyperglycemia in non-diabetic rabbits without affecting epinephrine-induced hyperglycemia. Chronic administration of the extract for six weeks also showed no effect on fasting blood glucose level. However, ethanol extract administered orally twice daily for 14 days to streptozotocin induced diabetic rats significantly reduced fasting serum glucose and increased body weight in a dose-dependent manner. The extract also significantly lowered levels of thiobarbituric acid-reactive substances in liver and kidney compared to vehicle-treated rats while significantly increasing the activity of superoxide dismutase and catalase enzymes and hepatic glutathione concentrations in diabetic rats [30].

Effects on Reproductive systems- A number of animal studies report the effect of *A. paniculata* on male and female reproduction. Early reports of oral administration of powdered stem indicate an anti-fertility effect in male Wistar mice, but no impact on fertility in female mice [31, 32]. It has also been reported that administration of *A. paniculata* resulted in abortion in pregnant rabbits. Intraperitoneal injection of the decoction of aerial parts to female albino mice was reported to prevent implantation and caused abortion at different gestation periods. Early pregnancy was also terminated by the intramuscular, subcutaneous and intravenous administration. Administration of progesterone or luteinizing hormone-releasing hormone completely or markedly antagonized the abortifacient effects, indicating interference with progesterone activity as a potential mechanism for this abortifacient effect. In addition, the herb is reported to suppress the growth of human placental chorionic trophoblastic cells *in vitro* condition [33].

Dysentery and Gastroenteritis- Previous studies conducted in China have reported the therapeutic value in acute bacillary dysentery and gastroenteritis 88.3% of acute bacillary dysentery and 91.3% of acute gastroenteritis cases has been cured by ethanol extracts andrographolide administration was reported to cure 91% of acute bacillary dysentery cases. The same cure rate (91.1%) was also achieved with a compound tablet containing andrographolide and neo-andrographolide at a ratio of 7:3 in cases of bacillary dysentery [34].

Antiviral Effects- Several studies on medicinal plant extracts have shown the antiviral activities against some RNA and DNA viruses. *A. paniculata* exhibits a neutralizing activity against the human immunodeficiency virus (HIV) [35]. Andrographolide was investigated for antiviral activity against herpes simplex virus (HSV) [36,37] HIV [38], flaviviruses and pestiviruses [39]. It has been demonstrated that 25 µg/ml of ethanolic extract of *A. paniculata* and 5 µg/mL of andrographolide effectively inhibit the expression of Epstein-Barr virus (EBV) lytic proteins, Rta, Zta and EA-D during the viral lytic cycle in P3HR1 cells [40]. A recent study has demonstrated that *A. paniculata* is the most antiviral inhibitory effects among six medicinal plants tested against DENV1-infected Vero E6 cells [41].

Anti-HIV effects- The growing incidence of drug-resistant HIV strains are one of the main problems in treating HIV infection. Although, current anti-HIV drugs can be inhibited the HIV infection. To avoid existing therapeutic difficulties, current searches for new anti- HIV agents are focused on discovering compounds with novel structures and different mechanisms of action as well as for the development of new anti-HIV drugs several studies have begun worldwide in the past few years [42,43]. Natural products and their derivatives have long been invaluable as a source of therapeutic agents for the development of medicine. The development of anti-HIV drugs derived from natural products is an area of research in which considerable effort should be dedicated in the future [44].

Infectious diseases- *A. paniculata* have been used for the treatment of leptospirosis, pulmonary tuberculosis, tuberculous meningitis and acute pyelonephritis cases. It has been reported that the administration of andrographolide significantly improved the CD4+ lymphocyte count from a baseline mean of 405 cells/mm³ to 501 cells/mm³ in HIV-positive patients. *A. paniculata* has been also used for upper respiratory tract infections (URTIs).

It has been observed that the differences in the degree of therapeutic effect on the basis of the kind of preparation used as well as the duration of treatment. Pills (made from the whole powdered plant with water) and tablets (made from the water extract of the herb) produced aggregate effective rates of 88 percent and 61 percent in URTI respectively. A study of including 158

adult patients suffering from common cold used a standardized *A. paniculata* dried extract SHA-10 (1,200 mg/day) for five days. The results of the study show that the extract significantly decreased the intensity of the symptoms of tiredness, sleeplessness, sore throat and nasal secretion from the second day of the starts of the treatment. It has been reported that the commercial preparation of a standardized extract of *A. paniculata* in a fixed combination with *Eleutherococcus senticosus* (Kan Jang) has been tested in URTIs [5]. Intra-arterial or retrograde intravenous injections of this herb were effective in thrombo-angiitis obliterans, especially of "heat toxic type." Ten cases of viper bites were cured in 3-5 days by a compound formula that had *A. paniculata* as the chief constituent [6].

Respiratory tract infections- Treatments for RTIs are mainly symptomatic [45] and often include antipyretics, analgesics [46], mucolytics, expectorants, decongestants [47] as well as educational interventions [48]. *A. paniculata* has traditionally and has been used in Indian and Chinese herbal medicine. It is traditionally used as an antipyretic for relieving and reducing the severity as well as the duration of the symptoms of common colds and alleviating fever, cough, and sore throats, or as a tonic to aid convalescence after uncomplicated RTIs [49,50]. There is encouraging evidence to demonstrate the potential mechanistic for effects of *A. paniculata* for RTIs. The active constituents of *A. paniculata* include components such as the lactones, diterpene is commonly known as the andrographolides, which have shown anti-inflammatory, antiviral, anti-allergic, and immunostimulatory properties [51]. They inhibit platelet-activating factor mediated inflammatory response [52], reduces expression of pro-inflammatory proteins such as cyclooxygenase-2 [53,54], and demonstrates analgesic effects as well as antipyretic effects comparable to paracetamol [55]. Results in vitro study show that *A. paniculata* has also been found to be effective against avian influenza A (H9N2 and H5N1) and human influenza A H1N1 viruses by blocking the binding of viral hemagglutinin to cells [56] or by inhibiting H1N1 virus-induced cell death [57]. Data from the previous studies showed that *A. paniculata* in alone or in combination with *A. senticosus* is superior to placebo for reducing symptom severity in upper RTIs [58,59].

CONCLUSIONS

As a consequence of increasing demand for the herbal drug treatment of various ailments, plant drugs from the ayurvedic system are being explored globally. This has resulted in many research studies with varied results and hence there is a need to summarize them together. This review acts as a ready reference for biological activities of Indian medicinal plants *A. paniculata* to the scientific community, in specific to researchers and students looking for sources of knowledge of medicinal plants and leads for new bioactive compounds. It is to be kept in mind that the reported activity may be shown by either the whole plant or a part of the plant or a particular extract or isolated compounds. Andrographolide, which exhibits notable pharmacological activities have attracted the interest of numerous researchers. Because of its rational activity, numerous andrographolide derivatives have been synthesized for the development of biological activities. This review summarizes various experimental clinical as well as pharmacological activities of andrographolide, such as antioxidant, anti-inflammatory, anticancer, antimicrobial and parasitic, hepatoprotective, antihyperglycemic, and antihypoglycemic. Evidence from clinical studies suggests that andrographolide reduces HIV symptoms, uncomplicated upper respiratory tract infections, including sinusitis and the common cold, and rheumatoid arthritis. *A. paniculata* has shown some significant effects on blood pressure. Before *A. paniculata* can be used clinically in hypertensive conditions, further research must be conducted to expand the understanding of this plant and its constituents on blood pressure and its regulation. Many pharmacological studies have suggested potential effectiveness of the andrographolide in restricting the infarct size, maintaining cardiac function under experimental cardiac ischemic conditions, preventing platelet aggregation, and preventing restenosis after balloon angioplasty. Significant anti-hyperglycemic activity in diabetic rats has been observed with both water and alcohol extracts. Alcohol extract reduced the serum triglyceride levels highly significantly and better than metformin treatment (an extensively used antidiabetic drug). Both extracts increased activities of antioxidant. Better glucose utilization via up-regulation of GLUT483 and increased insulin release has also been proposed as mechanisms for the anti-hyperglycemic effect.

CONTRIBUTION OF AUTHORS

All authors have contributed equally.

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