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A REVIEW ON KALMEGHA ANDROGRAPHIS PANICULATA (BURM.F.) NEES

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Abstract:

Medicinal plants are the most important source of life saving drugs for the majority of the world's population. In India, herbal medicine has been the basis of treatment for various diseases and physiological condition in AYUSH system of Medicine. Andrographis paniculata (Burm.f.) Nees belongs to the Acanthaceae family and commonly known as the 'King of bitters'. In Ayurveda Kalmegha, Bhunimba and Kiratatikta plants are used as a substitute to one another. This medicinal plant traditionally used for the treatment of cold, fever, jaundice, laryngitis and several infectious diseases.

A. paniculata possess hepatoprotective, anti-inflammatory, immunostimulatory, antipyretic, antioxidant, hypotensive, antibacterial, anticancer activities. The medicinal value of this plant is due to the presence of active ingredients viz. andrographolide and neoandrographolide which are derivatives of diterpenoids. The objective of this study is to review the literature of A. paniculata based on both Ayurvedic text and modern experimental studies, Citing through various research articles pertaining to therapeutic benefits, chemical properties and pharmacological evaluation.

Keywords: Kalmegha, Bhunimba, Andrographis paniculata, Andrographolide

Introduction:

Ayurveda is a medical science that gives us a profuse knowledge of Dravyas or drugs which we get from plants, animals and minerals. The medicinal plants are the potential source of Ayurvedic medicines and а core component at primary health care level due to their availability, compatibility and

affordability.¹ As claimed by World Health Organization (WHO), 65%-80% community of developing countries is currently using medicinal plants as remedy against different diseases.² *A. paniculata*, popularly known as Kalmegha in Sanskrit, is widely regarded to be a beneficial plant due to its diverse medicinal applications. It belongs to the family Acanthaceae known as "king of bitters," and is abundant

throughout India.³ The therapeutic potential of A. paniculata is due to its immense effect on gastrointestinal, upper respiratory infections, fever, herpes, and a variety of other chronic and infectious diseases.³ The plant extracts showed potent hepatoprotective, vermicidal, analgesic, anti-inflammatory and immune enhancer activity.⁴ Kalmegha is described by Acharya Priyavrata Sharma in Priyanighantu 'Shatapushapadi under Varga' and used to treat Yakrutroga, Krimiroga, Kushtha and Jwara.⁵

Aims and Objectives:

The study was carried out with aim to review Kalmegha *A. paniculata* through various classical Ayurvedic texts and research articles pertaining to therapeutic benefits, chemical properties and pharmacological evaluation.

Materials and Methods:

This study was carried out by critical reviews from Ayurvedic classical text like Samhita, Nighantu, Dravyaguna text books etc related to Kalmegha, Bhunimba, Kirattikta, searching various medical databases like Pubmed, Google scholar, Dhara, Google Search etc.

Discussion:

Taxonomical classification of A. paniculata⁶

Kingdom	:	Plantae, Plants		A MARCEN AN
Subkingdom	:	Tracheobionta,		
		Vascular plants		
Super division	n :	Spermatophyta, Seed		MA
		plants		
Division	:	Angiosperma		
Class	:	Dicotyledonae		
Sub class	:	Gamopetalae		
Series	:	Bicarpellatae		VI VINCA
Order	:	Personales	4	
Tribe	:	Justicieae		
Family	:	Acanthaceae		
Genus	:	Andrographis		
Species	:	paniculata		
			NParks Flore/FeuroWite	

Vernacular names^{7,8}

Arabic: Quasabhuva, Assamese: Kalmegh, Bengali: Kalmegh, Chinese: Chuan Xin Lian, English: The Creat, King of Bitters, French: Chirette verte, Hindi: Kirayat, Kalpanath, Japanese: Senshinren. Sanskrit: Kalmegha, Bhunimba.

Ayurvedic Aspect

Acharya Priyavrata Sharma mentioned it in the 'Shatpushpadi Varga'. Vaidya Bapalal has mentioned Kalmegha in the "Vasadi Varga" in his Aadarsh Nidhantu. It is of Tikta rasa with Katu Vipaka and Ushna Veerya and Kapha-pitta doshahara properties and Deepan as Karma, so it is used in kapha paittik vikara. It is prominently used in the diseases of paachana samsthana, raktavaha samsthana and twakroga. In Priyanighantu, it has been discussed that Kalmegha has activities like Paachana, Swedana, Krimighna and Pittasaraka. So it has been spacious in Yakrutroga, Krimiroga, Kushtha, and Jwara.^{5, 9, 10}

कालमेघस्तु भूनिम्बो यवाकारफ़ल्स्तथा ।

सुतिक्त लघुरूष्णोः कफ़ पत्त वनाशनः ॥

दीपनःस्वेदनो द्नेयः क्रू मघ्नः पत्तसारकः । यक्रूद्रोगे क्रमौ कुष्ठे ज्वरे चासौ प्रशस्यते ॥ Sarang P. Lakhmale, V. B. Washimkar & Nikita Yewatkar प्रय निघन्टू, शतपुष्पादि वर्ग,श्लो. १३५-१३६, प. १००

Controversy:

The plant which is considered to be Kiratatikta in South India is identified as Kalmegha by North Indian Ayurvedic scholars. Bengali Vaidyas identify this plant as Yavatikta^{8,10}. It has been noted that A. paniculata is popularly known as Bhunimba in M.P. and Nagpur area and as *Chiravata* in the Bihar forest.¹¹ It is stated in that Kerala. according to "Pharmacognosy of Ayurvedic Drugs of Travancore - Cochin" book, two plants were used for Kiratatikta as A. paniculata, Nees, and Solanum indicum^{10.} Yavatikta, according to me it is A. paniculata Nees. It is Kalmegha of Bengal and Kariyatu of Gujarat. It cannot be identified as Saptala¹². There is one word "Saptalika" (Su. Chi. 18/34) but there the commentator treated as "Yavatikta" A. paniculata, Nees (Kalmegha.). Personally I would like it as the diminutive form of Saptala¹².

It is now very clear that Kiratatikta (*S.chirata*) is different from Kalmegha (*A. paniculata*). Bapalal and Thakuraji are of the openion that Yavatikta is *A. paniculata*.¹³ Yavatikta is synonym of

Shanhkini (*Cha. Ka. 11/3*), but Shanhkini itself is a controversial drug. Kalmegha word is now prevelling to *Andrographis* and now we have to accept that one.¹⁰ keeping the other controversies a side, one should realize the importance of *Andrographis* as a potent hepatoprotective and antifebrile agent.¹³

Botanical Description:

It annual, is an branched, herbaceous plant erecting to a height of 30-110 cm in moist shady places with stem acutely quadrangular, much branched, easily broken fragile texture stem. Leaves are simple, opposite, lanceolate, glabrous, 2–12cm long; 1–3cm wide with margin acute and entire or slightly undulated and upper leaves often bractiform with short petiole. Inflorescence of the plant is characterized as patent, terminal and axillary in panicle, 10-30 mm long; bract small; pedicel short. The flowers possess botanical features of calyx 5-particle, small, linear; corolla tube narrow, about 6 mm long; limb longer than the tube, bilabiate; upper lip oblong, white with a yellowish top; lower lip broadly cuneate, 3-lobed, white with violet markings; stamens 2, inserted in the throat and far exserted; anther basally bearded. Superior ovary, 2-celled; style far exserted. Capsule of the plant is erect, linear-oblong, 1–2 cm long and 2-5 mm wide, compressed,

longitudinally furrowed on broad faces, acute at both ends, thinly glandular hairy. Seeds are very small, subquadrate.⁶

Distribution:

It is found in Sri Lanka, Pakistan, Java, Malaysia, Indonesia and throughout India, specifically in Maharashtra, Karnataka, Uttar Pradesh, Tamilnadu, Andhra Pradesh and Madhya Pradesh. It is cultivated to some extent in Assam and West Bengal.⁹

Collection Method and Time:

Ayurvedic science gives great importance on the collection methods of the drugs. Time has its own importance in the procedure involved. The whole plant material (Panchanga) of Kalmegha is used for its medicinal properties. It is collected when the entire plant is well grown and has full potency in the end of the rainy season (Varsha Ritu) or in the beginning of the winters (Sharad Ritu).¹

Formulations and Dosage:

In Ayurveda, Kalmegha is used in the form of many formulations such as Churna kalpna (powder form) 1-3 gms; Swaras (juice): 5-10 ml; Kwath (decoction): 20-40 ml; Taral satva (liquid extract): 1/2-1 ml.¹

Chemical Constituents:

Andrographolide,

Neoandrographolide, Andrograpanin, 1-2 didehydroandrographolide are the principal chemical constituents found in the plant.¹

Pharmacological Activities: Hepatoprotective Effects:

A. *paniculata* is extensively used as a hepatoprotective agent in Indian systems of medicine. It is also an ingredient in several polyherbalpreparations used as hepatoprotectants in india, one of which has been reported as efficacious in chronic hepatitis B virus infection. Most studies for hepatic effects have been conducted. Shukla et al reported significant choleretic effects of andrographolide in rats and guinea pigs. " Multiple-dose pretreatment with arabinogalactan proteins and andrographolide was protective against ethanol induced hepatotoxicity in mice and was deemed comparable to the efficacy of silymarin. Chowdhury and poddar reported that oral preand post-treatment of adult rats with an extract of A. paniculata was protective against ethanol-induced increase in serum transaminase. Administration of the extract to normal adult rats in single and multiple doses for seven and 15 days significantly did not affect serum transaminase. A comparative study on the effect of leaf extract or andrographolide on

carbon tetrachloride (Ccl₄) induced hepatic microsomal lipid peroxidation revealed a protective effect of a single oral dose of extract and of andrographolide. the However, high concentration ccl4-induced microsomal lipid peroxidation in vitro was completely protected by the extract but not by andrographolide, indicating that the hepatoprotective effect is not solely due to the presence of andrographolide. Hepatoprotective effects of the crude. Handa and sharma compared andrographolide, methanol extract of the whole plant containing equivalent amounts of andrographolide and an andrographolide-free methanol extract against Ccl4-induced liver damage in rats. "Ccl4-induced increases in serum transaminase, serum alkaline phosphatase, serum bilirubin, and hepatic triglycerides were inhibited by 48.6-, 32- and 15 percent, for andrographolide, methanol andrographolide-free extract. and methanol extract, respectively. Since all three treatments resulted in improvement in liver histology. Trivedi et al observed protection by both the crude extract of andrographis paniculata and andrographolide against reduced activities of hepatic antioxidant enzymes dismutase, (superoxide catalase, and glutathione peroxidase), depletion of glutathione, hepatic and increased activities of hepatic glutamyl

transpeptidase. glutathione-s-transferase, and lipid peroxidase caused by hexachlorocyclohexane in mice. Oral or ip. Pretreatment with andrographolide was also protective against galactosamineinduced liver damage in rats and prevented changes in biochemical parameters and liver histology. Similar protection was observed when rats were treated with andrographolide post acetaminophen challenge and on an ex vivo preparation of isolated rat hepatocytes. Various extracts and constituents of A. paniculata was used in the experiments mentioned in this subsection. All showed hepatoprotective effects. of A. Paniculata and also showed benefits against liver damage caused by agents with different hepatotoxic mechanisms.14

Immunostimulatory Activity:

Intragastric administration of an ethanol extract of the aerial parts (25mg/kg body weight) or purified andrographolides (1mg/kg body weight) to mice stimulated antibody production and the delayed-type hypersensitivity response to sheep red blood cells. The extract also stimulated a non-specific immune response in mice, measured by macrophage migration index, phagocytosis of [14c] leucine-labelled E. coli. proliferation of and splenic The extract was more lymphocytes. effective than either andrographolide or

neoandrographolide alone, suggesting that other constituents may be involved in the immunostimulant response.^{7,9}

Antimalarial Activity:

Chander R has concluded that 50% ethanolic extract of the aerial parts inhibited the growth of *Plasmodium* berghei both in vitro (100 mg/ml) and in mice after intragastric administration (1g/kg)body weight). Intragastric administration of a 1-butanol, chloroform or ethanol-water extract of the aerial parts to mastomys natalensis inhibited the growth of *P. berghei* at doses of 1–2 g/kg body weight. Bhaumik et al reported that andrographolide (5 mg/kg body weight) and neoandrographolide (2.5mg/kg body also effective weight) were when administered by gastric lavage.9

Antipyretic Activity:

Intragastric administration of an ethanol extract of the aerial parts (500mg/kg body weight) decreased yeastinduced pyrexia in rats. The extract was reported to be as effective as 200 mg/kg body weight of aspirin, and no toxicity was observed at doses up to 600 mg/kg body weight. Intragastric administration of andrographolide (100 mg/kg body weight) to mice decreased brewer's yeast-induced pyrexia. Intragastric administration of deoxyandrographolide, andrographolide,

neoandrographolide or 11, 12 didehydro-14-deoxyandrographolide (100 mg/kg body weight) to mice, rats or rabbits reduced pyrexia induced by 2, 4dinitrophenol or endotoxins.⁹

Antioxidant Effects:

Verma n et al. has been proved the antioxidant effects of the aqueous extract on liver defense systems in lymphoma bearing mice. The aqueous extract and alcoholic extract of Hydro the Α. showed increase paniculata the in activities of enzymes like catalase, superoxide dismutase and glutathione-s and reduced transferase lactate dehydrogenase activity. The results performed with that of aqueous extract of A. paniculata exhibited a greater antioxidant activity than the ethanolic extract in all model systems tested. Ojha sk et al. Resulted that the hydro alcoholic extract of A. paniculata possesses oxidative alterations in myocardium and confers substantial cardio protective activity by facilitating in retaining the cardiac function in a normal manner.⁹

Anti-inflammatory Activity:

A. paniculata inhibit the production of inflammatory mediators and alleviate acute hazards at its optimal dosages. Shen *et al.* observed that the andrographolide, an active component of

inhibits inflammatory Α. paniculata, responses by rat neutrophils. It was also found to inhibit the tumor specific angiogenesis by regulating the production of various pro and antiangiogenic factors by in vivo and in vitro studies. In a study by wang et al. A. paniculata was found to alleviate atherosclerotic artery stenosis induced by deendothelialization and high cholesterol diet as well as lower restenosis rate after experimental angioplasty. Further in a research by Coon *et al*. It was also found to be safe and efficacious for the relief of symptoms of uncomplicated upper respiratory tract infection.⁷

Antiulcer Activity:

Apigenin-7.4'-di-o-methyl ether produced significant dose dependent antiulcer activity in shay rats, histamineinduced ulcer in guinea pigs and in aspirininduced ulcers in rats (IJPS.1981, 43, 159).¹³

Antibacterial Activity:

An ethanol extract of the leaves inhibited the growth in vitro of *E. coli* and *staphylococcus aureus*. A 50% methanol extract of the leaves inhibited growth in vitro of proteus vulgaris. However, no in vitro antibacterial activity was observed when dried powder from the aerial parts was tested against *E. coli*, *Staphylococcus*

aureus, *Salmonella typhi* or *Shigella* species.^{9,7}

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Antivenom Activity:

Intraperitoneal injection of an ethanol extract of the aerial parts (25 g/kg body weight) to mice poisoned with cobra venom markedly delayed the occurrence of respiratory failure and death. The same extract induced contractions in guinea pig ileum at concentrations of 2 mg/ml. The contractions were enhanced bv physostigmine and blocked by atropine, but were unchanged by antihistamines. These data suggest that extracts of the aerial parts do not modify the activity of nicotinic receptors but produce the significant muscarinic activity, which accounts for its antivenom effects.¹⁵

It is used as curative or preventive in snake venom poisoning (I.M.J. 1963, 57, 307)¹³

Anti-ischemic Activity:

Total roots flavonoids effective against experimentalmyocardial ischemic necrosis induced by isoprenalinein rats and by ligation of leftdescending coronary artery in rabbits; decrease infraction size, and pathological changes in ST segment and Q wave inhibited; LD_{50} of flavonoids in mice, 1.15g/kg, i.v. (Zhongcaoyao. 1987, 18, 315)¹³

Anti-diarrhoel Activity:

Alcoholic extract of plant exhibited anti-diarrhoel activity against *E.coli* enterotoxins in animal models (IJCDR. 1990, 28, 273)¹³

Anti-human Immunodeficiency Virus (HIV) Activity:

Aqueous extracts of the leaves inhibited HIV-1 infection and replication in the lymphoid cell line molt-44. A hot aqueous extract of the aerial parts reduced the percentage of HIV antigen-positive h9 cells5. Dehydroandrographolide inhibited hiv-1 and hiv-1 (ucd123) infection of h9 cells at 1.6mg/ ml and 50mg/ml, respectively, and also inhibited hiv-1 infection of human lymphocytes at 50mg/ml6. A methanol extract of the leaves suppressed syncytia formation in co-cultures of uninfected and hiv-1infected molt cells median effective dose (ED_{50}) 70 mg/ml.¹⁵

Conclusion:

AYUSH system of medicine mostly deals with medicinal plants in treating variety of diseases and giving health to all. Kalmegha i.e. A. paniculata is such a medicinal plant found in abundant in nature and fulfilling the global demand of human population. Α. paniculata has been treating various diseases and which are highly showing preventative effects against ailments like liver damage, infection, hyperglycemia, cancer, etc. Andrographolide, is labdane diterpenoid having a diversity of pharmacological effects specified in indigenous system of medicine. Therefore, in future more clinical studies must be carried out for developing potent herbal formulations of A. paniculata as a major ingredient to treat variety of disease.

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