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Phytochemical and Pharmacological Activities of *Andrographis Paniculata* Nees. : A Review

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Abstract: ***Andrographis paniculata is well known as king of bitters and has wide range of medicinal pharmacological application, which has been use either single or in combination with other drugs in various Indian traditional systems of medicine like Unani, Ayurveda and Sidda. It exhibits anti-inflammatory, anti-HIV, anti- bacterial , anti-oxidant, nematocidal etc. Apart from having several active chemical constituents, andrographolide, neoandrographolide and dehydro-andrographolide are most important bioprotectants with wide range of therapeutic applications. The extract of Andrographis paniculata its wide range of applications in various fields, an attempt has been made in this review paper to explore various phytochemical and pharmacological studies carriedout on this drug.***

Keywords: *Andrographis paniculata*, *Kalmegh*, anti-inflammatory activity, andrographolides, biological activities, Toxicity.

1. Introduction

Andrographis paniculata belongs to the family Acanthaceae . It is distributed in tropical Asian countries, often in isolated patches. This species can be found in a variety of habitats, like plains , hill slopes, wastelands, farms, dry or wet lands, sea shores and even road sides. South India and Sri Lanka which are considered as centre of origin and diversity of the species for native populations. The herb is also available in northern parts of India, Java, Malaysia, Indonesia, West Indies and whereas in America where it is probably an introduced species. (Abhishek *et.al*.2010) The species also occurs in Hong Kong, Thailand, Brunei, and Singapore, etc. However, precise data are lacking on the introduction and naturalization of the species in these countries (Chopra *et.al*.1956; Prajapati *et.al*.2003)

The genus *Andrographis* Wall. Consists of 28 species among which *Andrographis paniculata* is the most popular as medicinal plant. It has been used as medicinal herb for centuries in several traditional systems of medicine all over the world. It is extensively used in Ayurveda, Unani and Siddha medicines as home remedy for various diseases in Indian traditional system as well as in tribal medicine in India and some other countries for multiple clinical applications. The therapeutic value of *Kalmegh* is due to its mechanism of action by enzyme induction. It is an important cold property herb, used fevers and to dispel toxins from the body. It is used to treat gastrointestinal tract and upper respiratory infections, fever, herpes, sor throat, hepatitis and a variety of other chronic and infectious diseases (Chopra *et.al*.1956) It exhibits antibacterial, antimalarial, filaricidal, antidiarrhoeal, cardiovascular activities, fertility effects and protection of liver and gallbladder. The herb and its isolates like andrographolide, neoandrographolide, dehydroandrographolide, isoandrographolide, etc. (Abhisek *et.al*.2010) are reported to possess anti-inflammatory, hepatoprotective, astringent, anodyne, tonic, alexipharmic and anti-pyretic properties and helps in arresting dysentery, cholera, diabetes, influenza, bronchitis, swellings and itches, piles and gonorrhea (Prajapati *et.al*.2003) Flavonoids, a diterpenoid demonstrated moderate vasorelaxing effect in isolated rat thoracic aorta (Wuts *et.al*.2008) The plant is used as an important ingredient in different medicinal formulations in national and international market.

2. Vernacular names:

Arabic	: Quasabhava
Bengali	: Kalmegh
English	: The creat
Gujarathi	: Kariyatu
Hindi	: Kirayat, Kalpanath
Kannada	: Nelaberu
Malayalam	: Nelavepu, Kariyattu
Marathi	: Oli-Kiryata
Oriya	: Bhuinimba
Persian	: Naine-havandi
Sanskrit	: Kalmegh, Bhunimba
Tamil	: Nilavembu
Telugu	: Nilavembu

Important Formulations

Important Ayurvedic formulations present in Kalmegh are as follows :
Gunna (properties/ laghu (light and ruksh (dry)
Rasa (taste) - tickta (bitter)
Virya (potency) – Ushan (hot)

Therapeutic Actions: The therapeutic value of kalmegh is due to its mechanism of action by enzyme induction. Kalmegh possess a number of therapeutic actions which mainly include anti-inflammatory, anti-pyretic hepatoprotective, astringent, anodyne, tonic, alexipharmic and helps in arresting dysentery, cholera, diabetes, influenza, bronchitis, swellings and itches, piles and gonorrhoea (Prajapati, *et.al*.2003) of the aqueous extract was clinically proved.

Therapeutic Uses: *Andrographis paniculata* recommended for prominent 26 Ayurvedic formulations treatment of various ailments include immunostimulant (Puri *et.al*. 1993) asthma, gonorrhea, piles (Rao 1914) dysentery and dyspepsis (Bhalla *et.al*.1982) blood purification (Vohora, 1985) influenza (Dey, 1986) gastric complaints, diarrhea (Gupta *et.al*. 1990) pharyngitaonsillitis (Thamlikitkal, *et.al*

1991) fever, (Ahmad, *et.al*. 1992) loss of scalp hair, (Home *et.al*.1992) Snake bite (Gupta et.al. 1994), myocardial ischemia, (Guo *et.al*. 1995) common cold (Melchior, *et.al*. 1996), diabetes (Zhang, *et.al*.2000), respiratory tract infections (Coon, *et.al*.2004), Jaundice (Tomar, *et.al.*1983), antiulcerogenic, (Viswanathan, *et.al*. 1981) antityphoid (Anonymous 1985), antisnake venom (Selvanayagam, *et.al*. 1994), antifertility (Akbarsha *et.al.* 2000), anti-inflammatory (Shen *et.al*. 2002), and antihyperglycemic (Rao *et.al*. 2006). Apart from it shows bioeffectivity of the species against phytopathogens (bacteria, fungi) suggested the utility of the species in development of novel broad spectrum antimicrobial agents.

3. Morphology

Macroscopic

Andrographis paniculata is an annual, branched, erect, grows up to 1m height. It is distributed in tropical Asian countries , often in isolated patches. It can be found in a variety of habitats, e.g. plains, hill slopes. Wastelands, farms, dry or wet lands, sea shores and even road sides. The aerial parts of leaves, and stems are used to extract the active phytochemicals. Stem sharply quandrangular in shape, leaves simple, opposite lanceolate acute at both ends glabrous, 5-8 cm long, 1-2 cm wide, entire, upper surface is dark green, pale beneath, main nerves 4-6 pairs, Inflorescence terminal or axillary panicle flowers small, white with purplish or violet markings, , calyx 5, partite, pubescent, corolla bilabiate, hairy upper lip oblong, lower lip 3 lobed calyx lobes glandular, stamens 2, declinate, inserted in the throat, filaments epipetalous, ovary 2 celled, fruit capsules, linear oblong, two celled, compressed, longitudinally furrowed on broad faces, acute at both ends, glandular-hairy. Seeds small, seeds numerous, yellowish brown, subquadrate , round or ovoid, yellowish brown. Root is cylindrical, curved, tapers, 5-20 cm long and 1.5 - 5cm in diameter. Externally it is grayish brown, when fractured the inside is starchy white.

Microscopic

Stem single layered epidermis, just beneath 2-3 layered collenchyma with secretary cavities and with white coloured deposition. Cortex 5-6 layers contain chloroplast. Solitary and group of sclereids of 4-6 are present in cortex. Thick walled endodermis. Solitary sclereids are present in secondary phloem tissues. Xylem very prominent and occupies major portion. Tyloses are occasionally found in cells of xylem vessels and pith cells contains prismatic crystals of calcium oxalate.

Phytochemical Studies

A review of the literature reveals that the presence of various chemical constituents in the aerial parts of the *Andrographis paniculata* are andrographolide, which is diterpene lactone, colourless, crystalline, bitter in taste (Abhishek *et.al*.2010). Other compounds include 14-deoxy-11-oxoandrographolide, didehydro andrographolide/andrographlide D, 14-deoxyandrographolide, non-bitter compound is neo andrographolide, homoandrographolide, andrographosterin, andrograpanin, α-sitosterol, stigmasterol. Apigenin-7, 4-di-o-methyl ether, 5-hydroxy 7,8,2, 3-tetramethoxy flavones, monohydroxy trimethyl flavones, andrographin, dihydroxy-di-methoxy flavoue, panicolin, andrographoneo, andrographoside, andropani-culoside A (3, 7, 8) andrograpanin, Isoandrographolide and skollcaflavone (9-12). Six entlabdane diterpenoids i.e. 3-o-beta-D-glucopyranosyl-14, 19-dideoxyandrographolide, 14-deox, 17-hydroxyandrographolide, 19-o-[beta-D-apiofuranosy 1-2-beta-D-glucopyranoyl]-3, 14-dideoxyandiographolide, 3-o-beta-D-glucopyranosyl-andro-grapholide, 12S-hydroxy andrographolide and andrographatoside. These compounds showed inhibitor activity against several fungal and bacterial strains.

Dua *et al.* (2004) reported four xanthones 1,8-dihydroxy-3,7-dimethoxy xanthone, 4,8-di-hydroxy-2, 7-dimethoxy-xanthones, 1,2-dihydroxy-6, 8-dimethoxyxanthone and 3,7,8-trimethoxy-1-hydroxyxanthone from the roots.

Pharmacological studies

Pharmacological activity of the Kalmegh is mainly attributed to the presence of andrographolide, neoandrographolide, etc. It is further reported that these species shows presence of flavonoids, diterpenoids, etc.

Antidiabetic activity:

Antidiabetic property of *A paniculata* was confirmed by Borhanuddin *et al.* (1994) and Husen *et al.* (2004) in aqueous extract and by Zhang *et al* .(2000) in ethanolic extract. Along with antihyperglycaemic property, the ethanolic extract may also reduce oxidative stress in diabetic rats as studied by Zhang *et al.* (2000). Further, it was concluded by Yu BC *et al.* in 2003 that the andrographolide was responsible for the antihyperglycemic activity. Finally in 2006, the antidiabetic potential of *A. paniculata* was found to restore impaired estrous cycle in alloxan-induced diabetic rats (Reyes *et.al*. 2006).

Anti-inflammatory activity:

A. paniculata can also inhibit the production of inflammatory mediators and alleviate acute hazards at its optimal dosages (Chao *et.al*. 2011). Shen *et al.* in 2002 observed that the andrographolide, an active component of *A. paniculata,* inhibits inflammatory 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 (Sheeja *et.al*. 2007). In a study by Wang *et al.* (1994) *A. paniculata* was found to alleviate atherosclerotic artery stenosis induced by both deendothelialization and high cholesterol diet as well as lower restenosis rate after experimental angioplasty. Further in a research by Coon *et al.* in 2004 it was also found to be safe and efficacious for the relief of symptoms of uncomplicated upper respiratory tract infection. Poolsup *et al.* and Gabrielian *et al.* in their double-blind clinical study also proved that *A. paniculata* extract alone or in combination may be more effective than placebo and may be an appropriate alternative treatment of uncomplicated acute upper respiratory tract infection (Coon *et.al*. 2004) Immunological and biochemical studies were carried out in 2006 by Sheeja *et al.* to investigate protective effects of ethanolic extract of *A. paniculata* against cyclophosphamide

(CTX)-induced toxicity *in vivo.* Histopathological analysis of small intestine also suggests that extract could reduce the CTX-induced intestinal damage.

Antoxidant activity:

Sheeja *et al.* (2006) concluded that the methanolic extract of *A. paniculata* was found to inhibit the formation of oxygen derived free radicals such as superoxide (32%) hydroxyl radicals (80%), lipid peroxidation (80%), and nitric oxide (42.8%) in *in vitro* system. Trivedi et al. studied the effect of the *A. paniculata* on antioxidant activity in mice by using the enzymes y-Glutamyl transpeptidase, glutathione-S-transferase, and lipid peroxidation compared to Benzenehexa Chloride (BHC). The activities of antioxidant enzymes like superoxide dismutase, catalase, glutathione peroxidase, and the levels of glutathione were decreased following the BHC effect.

Hepatoprotective activity:

In 1993, Visen *et al.* found that andrographolide has a significant dose-dependent protective activity against paracetamol-induced toxicity on ex vivo preparation of isolated rat hepatocytes. Kapil *et al.* (1993) proved effects of *A. paniculata* on hepatotoxicity induced in mice by carbon tetrachloride.

Immuno-modulatory activity

In 1993, Puri *et al.* reported that the ethanolic extract and purified diterpene andrographolides of *A. paniculata* (Acanthaceae) induced significant stimulation of antibody and delayed type hypersensitivity (DTH) response to sheep red blood cells (SRBC) in mice. Rajagopal *et al.* in 2003 suggest that andrographolide is an interesting pharmacophore with anticancer and immunomodulatory activities. Further, in 2004, a positive anticancer and immunomodulatory activity of the methanolic extract were screened Kumar *et al.* for human cancer and immune cells. In 2005 Cheung *et al.*carried out the in vitrocytotoxicities of the ethanolic extract of *A. paniculata* (APE) and its main diterpenoid components evaluated in various cancer cells. APE was found to be significantly growth inhibitory to human acute myeloid leukemia HL- 60 cells with an IC (50) value of 14.01 ug/ml after 24 hours of treatment. Wiart *et al.* found that some isolated compounds, i.e. Andrographolide, neoandrographolide, and 14-deoxy-11, 12- didehydroandrographolide, ent-labdene diterpenes showed viricidal activity against herpes simplex virus 1 (HSV-1). Further, aqueous extracts of A. *paniculata* are expected to be scorpion venom antidotes with low cytotoxicity. The production of interleukin-2 and interferon-gamma in normal and Ehrlich ascites carcinoma-bearing animals was elevated. latest by 2006 in an experimental study by Zhou *et al.*, it was shown that the key mediators in relaying the cell death signaling initiated by Andrographolide.

The facts that andrographolide is a nontoxic substance is evident from a recently reported toxicological study, 32 and is reconfirmed by the observations made in the pilot experiment described in this communication. By contrast, even the lowest andrographolide dose tested (3 mg/kg/d) completely prevented the daily handing- and intermittent foot-shock-triggered body weight losses, and the slight elevation of core body temperatures within physiological ranges observed in control animals. Moreover, dose- and treatment regimen-dependent partial protection against transient foot-shock-triggered hyperthermia, with ED50 values around 10 mg/kg/d, was observed in the pilot as well as in both the confirmatory experiments. Because the dose and duration of treatment dependence of these observed effects of andrographolide were not identical, it seems reasonable to assume that different physiological thermoregulatory mechanisms and biological process are involved in its diazepam-like beneficial effects observed only after their fairly low daily oral doses.

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