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Medicinal and Pharmacological Activities of *Andrographis paniculata* – Review

S. Meenatchisundaram*, G. Parameswari, T. Subbraj, T. Suganya and A. Michael

Department of Microbiology, PSG College of Arts and Science, Coimbatore, India
*Corresponding author. Ph: +91- 422 -09842525152 E.Mail:drmscbe@gmail.com

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Introduction

Andrographis paniculata is a herbaceous plant in the family *Acanthaceae,* native to India and Sri Lanka. It is widely cultivated in southern Asia, where it is used to treat infections and some diseases, often being used before antibiotics were created. Mostly the leaves and roots were used for medicinal purposes. *Andrographis paniculata* is used in traditional Siddha and Ayurvedic systems of medicine 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 which is perhaps by enzyme induction. The plant extract exhibits antityphoid and antifungal activities. Kalmegh is also reported to possess antihepatotoxic, antibiotic, antimalarial, antihepatitic, antithrombogenic, antiinflammatory, antisnakevenom, and antipyretic properties to mention a few, besides its general use as an immunostimulant agent.

Antibacterial activity

An ethanol extract of the leaves inhibited the growth in vitro of *Escherichia coli* and *Staphylococcus aureus*[1]. A 50% methanol extract of the leaves inhibited growth in vitro of *Proteus vulgaris*[2]. 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[3].

Anti-human immunodeficiency virus (HIV) activity

Aqueous extracts of the leaves inhibited HIV-1 infection and replication in the lymphoid cell line MOLT-4[4]. A hot aqueous extract of the aerial parts reduced the percentage of HIV antigen-positive H9

cells[5]. 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/ml[6]. A methanol extract of the leaves suppressed syncytia formation in co-cultures of uninfected and HIV-1-infected MOLT cells (median effective dose [ED50] 70mg/ml) [7].

Immunostimulatory activity

Intragastric administration of an ethanol extract of the aerial parts (25mg/kg body weight) or purified andrographolides (1 mg/kg body weight) to mice stimulated antibody production and the delayed-type hypersensitivity response to sheep red blood cells[8]. The extract also stimulated a non-specific immune response in mice, measured by macrophage migration index, phagocytosis of [14C] leucine-labelled *E. coli*, and proliferation of splenic lymphocytes[9]. The extract was more effective than either andrographolide or neoandrographolide alone, suggesting that other constituents may be involved in the immunostimulant response[10].

Antipyretic activity

Intragastric administration of an ethanol extract of the aerial parts (500mg/kg body weight) to rats decreased yeast-induced pyrexia[11]. 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[12]. Intragastric administration of andrographolide (100 mg/kg body weight) to mice decreased brewer's yeast-induced pyrexia[13]. 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 2,4-dinitrophenol or endotoxins[14].

Antidiarrhoeal activity

Herba Andrographidis has antidiarrhoeal activity in situ[15]. An ethanol, chloroform or 1-butanol extract of the aerial parts (300mg/ml) inhibited the *E. coli* enterotoxin-induced secretory response-which causes a diarrhoeal syndrome- in the rabbit and guinea-pig ileal loop assay[15]. However, an aqueous extract of the aerial parts was not active[16]. The constituent diterpene lactones, andrographolide and neoandrographolide, exhibited potent antisecretory activity in vivo against *E. coli* enterotoxin-induced diarrhoea[16]. Andrographolide (1 mg per loop) was as active as loperamide when tested against heat-labile *E. coli* enterotoxin-induced diarrhoea and more effective than loperamide when tested against

heat-stable *E. coli* enterotoxin-induced diarrhoea[16]. Neoandrographolide (1 mg per loop) was as effective as loperamide when tested against heat-labile *E. coli* enterotoxin-induced diarrhoea and slightly less active than loperamide when tested against heat-stable *E. coli* enterotoxin-induced diarrhoea[16]. The mechanism of action involves inhibition of the intestinal secretory response induced by heat-labile *E. coli* enterotoxins, which are known to act through the stimulation of adenylate cyclase, and by inhibition of the secretion induced by heat-stable *E. coli* enterotoxins, which act through the activation of guanylate cyclase[15]. Incubation of murine macrophages with andrographolide (1–50mol/l) inhibited bacterial endotoxin-induced nitrite accumulation in a concentration- and time dependent manner[17].

Anti-inflammatory activity

Intragastric administration of deoxyandrographolide, andrographolide, neoandrographolide or 11,12-didehydrodeoxyandrographolide to mice inhibited the increase in cutaneous or peritoneal capillary permeability induced by xylene or acetic acid, and reduced acute exudation in Selye granulocysts treated with croton oil. 11,12-Didehydrodeoxyandrographolide had the most potent anti-inflammatory activity in vivo[17]

Antimalarial activity

A 50% ethanol extract of the aerial parts inhibited the growth of *Plasmodium berghei* both in vitro (100 mg/ml) and in mice after intragastric administration (1 g/kg body weight) [18]. 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[19]. Andrographolide (5 mg/kg body weight) and neoandrographolide (2.5mg/kg body weight) were also effective when administered by gastric lavage[19].

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[17]. The same extract induced contractions in guinea-pig ileum at concentrations of 2 mg/ml. The contractions were enhanced by physostigmine and blocked by atropine, but were unchanged by antihistamines[17]. These data suggest that extracts of the aerial parts do not modify the activity of the nicotinic receptors but produce significant muscarinic activity, which accounts for its antivenom effects[17].

Antihepatotoxic activity

The aerial parts and their constituent andrographolides have antihepatotoxic activity in vitro and in vivo[21]. Intraperitoneal administration of a methanol extract of the aerial parts (861.3 mg/kg body weight) to mice reduced hepatotoxicity induced by carbon tetrachloride (CCl4), and reversed CCl4-induced histopathological changes in the liver[18,19]. Intraperitoneal administration of andrographolide (100 mg/kg body weight) to mice inhibited the CCl4-induced increase in the activity of serum glutamate oxaloacetate transaminase, serum glutamate pyruvate transaminase, alkaline phosphatase, bilirubin and hepatic triglycerides[20]. Intraperitoneal administration of a methanol extract of the aerial parts (500 mg/kg body weight) to rats also suppressed the CCl4-induced increase in the activity of serum glutamate oxaloacetate transaminase, serum glutamate pyruvate transaminase, alkaline phosphatase and bilirubin[18]. Intragastric administration of an aqueous extract of the aerial parts (500mg/kg body weight) to ethanol-treated rats decreased the activity of serum transaminases and suppressed histopathological changes in the liver[17]. Andrographolide, the major antihepatotoxic component of the plant, exerted a pronounced protective effect in rats against hepatotoxicity induced by CCl4, Dgalactosamine, paracetamol and ethanol. Andrographolide was more effective than silymarin, the standard hepatoprotective agent[18- 21].

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