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Andrographis Paniculata in the Treatment of Upper Respiratory Tract Infections

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ABSTRACT

Andrographis paniculata is a species of Andrographis paniculata (Burm. F) The herbaceous plant Nees, sometimes known as "king of bitters," is a member of the Acanthaceae family. It's commonly used to treat sore throats, flu, and upper respiratory tract infections in China, India, Thailand, and Malaysia. In numerous studies, andrographolide, a significant bioactive chemical ingredient of the plant, has shown anticancer potentialIn experimental models of asthma, stroke, and arthritis, andrographolide and its derivatives show anti-inflammatory properties. Pharmaceutical chemists have recently synthesized a number of andrographolide derivatives with important pharmacological properties such as anti-inflammatory, antibacterial, anticancer, antidiabetic, anti-HIV, antifeedant, and antiviral properties. The summary of the effects of andrographolide on cardiovascular illness, platelet activation, infertility, and NF-B activation in this research is remarkable. In traditional Indian and Chinese medicine, a variety of plant items were frequently recommended as medications. We investigate the potency of four selected phytochemicals from the A. paniculata plant, namely andrographolide (AGP1), 14-deoxy 11,12-didehydro andrographolide (AGP2), neoandrographolide (AGP3), and 14-deoxy andrographolide (AGP4), against four key targets, including three non-structural protein (3 L main protease (3CLpro), Papain like proteinase (PLpro) and RNA-directed RNA polymerase (RdRp)) and a structural protein (spike protein (S)) of the virus which are responsible for replication, transcription and host cell recognition. This paper intended to know the mechanism of A.Panniculata bioactive compounds and its effect to relief the upper respiratory tract infection symptomps.

1. Introduction

Upper respiratory tract infections are described as self-limited irritation and swelling of the upper airways with accompanying cough, with no evidence of pneumonia, no other condition to account for the patient's symptoms, and no history of COPD/emphysema/chronic bronchitis. Upper respiratory tract infections can be caused by a variety of viruses and bacteria. Acute bronchitis, the common cold, influenza, and respiratory distress syndromes are all caused by these bacteria. Because the symptoms of upper respiratory tract infections (URIs) frequently overlap and their causes are similar, defining most of these patient disorders is difficult. Upper respiratory tract infections involve the nose, sinuses, pharynx, larynx, and the large airways.[1] Rhinovirus is the most frequent virus. The influenza virus, adenovirus, enterovirus, and respiratory syncytial virus are among the other viruses. Bacteria may be the source of 15% of all sudden onset pharyngitis cases. S. pyogenes, a Group A streptococcus, is the most prevalent. Cough, sore throat, runny nose, nasal congestion, headache, low-grade fever, facial pressure, sneezing, malaise, and myalgia are frequent URTI symptoms. The onset of symptoms usually begins one to three days after exposure and lasts 7–10 days, and can persist up to 3 weeks.[1]

In Indonesia, respiratory tract infections (RTIs) are one of the most prevalent reasons for primary care visits. The purpose of cold treatment is to alleviate symptoms. Decongestants and antihistamine/decongestant combinations can help people with cough, congestion, and other symptoms. Antibiotics are not recommended for the treatment of the common cold since they do not relieve symptoms or shorten the duration of the disease, according to evidence. Research has suggested RTIs are predominantly of viral etiology, and that antibiotics are of very limited benefit in the majority of uncomplicated infections Antimicrobial resistance (AMR) is a growing global public health threat. Antibiotics' marginal benefit for ARTIs is offset by rising AMR and common adverse responses, resulting in unnecessarily high healthcare expenditures. To prevent excessive antibiotic prescribing, further research is needed to look into other treatments that may be administered for symptomatic relief. There has been a lot of interest in researching choices now available to the general public in order to assist speedy translation of research into clinical practice. Over-the-counter (OTC) pharmaceutical treatments like paracetamol, as well as natural alternatives, have been used. Evidence from previous systematic reviews suggested promising but limited evidence for Chinese herbs in influenza, common colds, upper RTI, and cough.[1]

A. Paniculata (Burm.f.) Wall ex Nees (Acanthaceae family), also known as nemone chinensi, Chuān Xīn Lián, has traditionally been used in Indian and Chinese herbal medicine. It has traditionally been used as an antipyretic to relieve the severity and length of symptoms of common colds, as well as to relieve fever, cough, and sore throats, or as a tonic to help convalescence after uncomplicated RTIs. There is promising data to support A. Paniculata's possible mechanistic effects on RTIs. The diterpene, lactones widely known as andrographolides, which have anti-inflammatory, antiviral, anti-allergic, and immune-stimulatory properties, are active elements of A. Paniculata. They suppress platelet-activating factor-mediated inflammation, diminish production of pro-inflammatory proteins including cyclooxygenase-2, and have analgesic and antipyretic properties comparable to paracetamol. *A. Paniculata* has also been shown, in vitro, to be effective against avian influenza A (H9N2 and H5N1) and human influenza A H1N1 viruses, possibly through blocking the binding of viral hemagglutinin to cells, or by inhibiting H1N1 virus-induced cell death.[2]

2. Discussion

Based on the result from the review studies, it shows that *Andrographis Panniculata* is effective against upper respiratory tract infections. The published evidence supports the usefulness of A. paniculata in reducing the severity of uncomplicated acute upper respiratory tract infection. This could be attributable to the anti-inflammatory, antipyretic activity, and immunomodulatory effects of andrographolide.[3]

Effects on antioxidant defense

A. paniculata and its components have been shown to have antioxidant properties in several investigations. The aqueous extract of A. paniculata increased the activities of antioxidant defense enzymes like catalase, superoxide dismutase, and glutathione-S-transferase while lowering glutathione level, according to Verma and Vinayak. The extract reduces lipid peroxidation by lowering thiobarbituric acid-reactive substances levels in the liver and kidney of diabetic rats (when compared to normal rats) and considerably increasing hepatic glutathione concentrations. The accumulation of the phorbol-12-myristate-13-acetate (PMA-) triggered generation of ROS and N-formyl-methionyl-leucyl-phenylalanine-phenylalanine-phenylalanine-phenylalanine-phenylalanine-phenylalanine-phenylalanine-phenylalanine-phenylalanine-phenylalanine-phenylalanine-phenylalanine- Andrographolide's ability to scavenge free radicals lowered oxidative stress and the production of thiobarbituric acid-reactive substances.[3]

Anti-inflammatory effects

Histamine, dimethyl benzene, and adrenaline have all been shown to produce inflammation, whereas andrographolide has been shown to greatly reduce

inflammation. Because of the expression of inducible isoforms of nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2), overproduction of NO and prostaglandin E2 (PGE2) plays a crucial role in the inflammatory processes of activated macrophages. The activation of iNOS by lipopolysaccharide stimulates and promotes the secretion of proinflammatory cytokines from macrophages, resulting in increased NO generation. The methanol extract of *A. paniculata* and andrographolide incubated with macrophages have been reported to inhibit LPS-stimulated NO production in a concentration-dependent manner. Chiou et al. observed that andrographolide inhibits lipopolysaccharide-induced nitric oxide (NO) production and inducible NO synthase (iNOS) expression in the murine macrophage-like cell line RAW 264.7. After incubation with LPS, andrographolide totally restored the maximal contractile response of the thoracic aorta to phenylephrine and relieved the drop in anesthetized rats' mean arterial blood pressure. Andrographolide has also been shown to limit dendritic cell maturation and antigen presentation, as well as suppress IL-2 production and T-cell proliferation in a mixed lymphocyte reaction.[3]

Immunomodulatory activity

Purified andrographolide (1 mg/kg body weight) or ethanol extracts of the stems and leaves (25 mg/kg body weight) administered intragastrically to mice stimulates antibody production and the delayed-type hypersensitivity reaction to sheep red blood cells. In addition, the extract and pure andrographolide were found to elicit an innate immunological response in mice, as indicated by the macrophage movement index, phagocytosis of leucine-labeled Escherichia coli, and splenic lymphocyte proliferation driven by A. paniculata extract. The immunomodulatory function of the diterpene lactone andrographolide has been linked to an increase in human peripheral blood lymphocyte proliferation, as well as the production of critical cytokines and the expression of Y Xu 21 immune activation markers in whole blood cells cultured in vitro. Rajagopal et al. and Kumar et al. found that andrographolide has immunostimulatory effect in PHA-stimulated human peripheral blood lymphocytes (HPBLs), as evidenced by enhanced cell proliferation and IL-2 production in vitro. *In mice treated with andrographolide, in vivo immunological responses such as an antibody response to a thymus-dependent antigen and delayed-type hypersensitivity were significantly reduced.* In addition, Iruretagoyena et al. found that andrographolide inhibited NF-kappa B activation in murine DCs, enhancing the tolerogenic capabilities of immature dendritic cells (DCs) in experimental autoimmune encephalomyelitis (EAE). In vitro, andrographolide has been shown to inhibit the production of IFN- and IL-2 in murine T cells activated with concanavalin A (Con A). Furthermore, andrographolide has been shown to decrease TNF- and IL-12 production in macrophages activated by lipopolysaccharide.[4]

Antimicrobial effects

Antimicrobial activity of A. paniculata and andrographolide has been reported against a variety of microbiological species. Even at a concentration of 25 mg/mL, the crude powder of A. paniculata was found to have antibacterial action against Salmonella, Shigella, E. coli, gram A streptococci, and Staphylococcus aureus in vitro. Singha et al. discovered that an aqueous extract containing andrographolide has strong antibacterial activity. A crude aqueous extract of leaves with substantial antibacterial activity against gram-positive S. aureus, methicillin-resistant S. aureus, and gram-negative Pseudomonas aeruginosa produced a comparable result. Significant activity against enterohemorrhagic strains of *E. coli* was found in the ethanol extract of *A. paniculata*. The virucidal activity of andrographolide has been reported against herpes simplex virus 1 (HSV-1) without having any significant cytotoxicity. At a concentration of 0.05 mg/mL of a chloroform extract of *A. paniculata,* the plant completely inhibits malarial parasitic growth within 24 h of incubation; and the same inhibition has been noted within 48 h with methanol extract concentration of 2.5 mg/mL. A methanol extract was found to inhibit *Plasmodium falciparum* substantially at a 50% inhibitory

concentration (IC50) of 7.2 μg/mL. The ethanolic extract of A. paniculata was found to be useful in the treatment of upper respiratory infections. Antimicrobial activity of A. paniculata against nine bacterial strains has also been reported, including Salmonella typhimurium, E. coli, Shigella sonnei, Staphylococcus aureus, Pseudomonas aeruginosa, Streptococcus pneumoniae, Streptococcus pyogenes, Legionella pneumophila, and Bordetella pertussis.[4]

Antiviral effects

Plant extracts' antiviral properties have been rediscovered and are the subject of intense scientific research. A number of medicinal plant extracts have been found to have antiviral properties against RNA and DNA viruses. A. paniculata is one of these plants, and it has antiviral efficacy against the human immunodeficiency virus (HIV). Antiviral activity of andrographolide was tested against herpes simplex virus (HSV), HIV, flaviviruses, and pestiviruses. Lin et al. 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. A recent study has demonstrated that *A. paniculata* has the most antiviral inhibitory effects among six medicinal plants tested against DENV1-infected Vero E6 cells.[4,5]

Inhibitory effects on NF-kappa B (NF-κB) transcription factors

Because NF-B plays such an important role in the pathophysiology of inflammation, several medications targeted to treat human inflammatory disease target NF-B activation. Many natural substances or herbal extracts are said to have anti-inflammatory properties, which are thought to be mediated by NF-B activation. Phytochemicals, particularly flavonoids, are gaining popularity due to their important biological and pharmacological effects, which include inhibiting NF-B activation. NF-kappa B is a family of inducible transcription factors that regulates the immunological and inflammatory responses of the host. The NF-kappa B transcription factor controls the expression of immune system components such as proinflammatory cytokines, chemokines, adhesion molecules, and inducible enzymes like cyclooxygenase-2 and inducible nitric oxide synthase, as well as proteins that regulate specific immune responses like interleukin-2, IL-12, and interferon- that control lymphocyte homing. As a result, inflammatory and autoimmune disorders can be caused by dysregulation of this transcription factor.[6,7]

Through the covalent alteration of decreased Cys62 of p50, andrographolide has been shown to alleviate inflammation by blocking NF-kappa B activation. Andrographolide produced a covalent adduct with a reduced cysteine of p50, preventing NF-kappa B oligonucleotide from binding to nuclear proteins. Andrographolide reduced the expression of the cell adhesion molecule E-selectin and blocked E-selectin-mediated leukocyte adherence in stimulated endothelial cells via suppressing NF-kappa B activation. PAF and fMLP induced DNA binding of NF-kappa B in whole cells and nuclear extracts was also decreased by andrographolide. As a result, andrographolide reduces the expression of proinflammatory proteins like COX-2 by decreasing NF-kappa B binding to DNA.[7]

Antipyretic and analgesic effects

A. paniculata is commonly utilized in Asian countries for its antipyretic, analgesic, protozoacidal, antihepatotoxic, anti-HIV, immunostimulant, and anticancer properties. Andrographolide, given in oral doses of 100 and 300 mg/kg, was found to have a strong antipyretic effect in rats after 3 hours of brewer's yeast-induced fever. Furthermore, andrographolide doses of 180 or 360 mg/kg were observed to alleviate fever in adults on the third day following administration. Madav et al. also found that 300 mg/kg of andrographolide, given orally, exhibited significant analgesic activity in mice and rats in the acetic-induced writhing test and the Randall-Selitto test, but no impact in mice in the hot plate test. These researchers also discovered that giving 4 mg/kg of andrographolide intraperitoneally had an analgesic effect, but giving 300 mg/kg orally had no

effect in the previous study. This variance could be due to the diverse administration routes used in this research.[5,6]

3. Conclusion

A. paniculata has long been used to treat upper respiratory infections (URTIs). Thamlikitkul et al. gave A. paniculata at a dose of 6 g/day for 7 days to 152 Thai adults with pharyngotonsillitis in a randomized, double-blind, and controlled study, and the efficiency was reported to be comparable to that of acetaminophen in treating the symptoms of fever and sore throat. In a duration-dependent man, Cáceres et al. clearly demonstrated that treatment with Andrographis paniculata extract SHA-10 reduces the intensity of tiredness (OR = 1.28; 95 percent CI 1.07–1.53), sleeplessness (OR = 1.71; 95 percent CI 1.38–2.11), sore throat (OR = 2.3; 95 percent CI 1.69–3.14), and HSP (OR = 2.51; 95 percent CI 1.82–3.46). They discovered that using Andrographis paniculata extract for four days reduced the severity of all symptoms much more than using it for two days. *Paniculata appears to be effective and safe for alleviating ARTI symptoms and reducing the time it takes for symptoms to resolve.* However, these findings should be interpreted cautiously owing to poor study quality and heterogeneity. A. Paniculata requires well-designed trials to assess its effectiveness and potential to minimize antibiotic use.[6,7]

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