

ANDROGRAPHIS

Andrographis paniculata (Burm.f.) Nees

Family

Acanthaceae, the acanthus family, typified by tropical herbaceous plants and shrubs with similar characteristics.

Parts Used

Herb.

Description

Andrographis is a small green, shade loving, annual shrub found throughout India and other Asian countries. Under cultivation it can reach up to a height of 30 to 110cm with shiny leaves that grow up to 8cm in length. The white, or pale pink, flowers are particularly beautiful but incredibly small and

have rose-purple spots on the petals. Its seed pods are yellow-brown, smooth and oblong in shape, approximately 2cm long.^{1,2}

Traditional Use

Commonly known as the 'king of bitters' and 'Indian echinacea', andrographis is an Ayurvedic herb that has been used traditionally for centuries as a bitter tonic to support the immune system, as a remedy against intestinal parasites and a general stomach tonic. It is also known as "bhui-neem" since it has a similar appearance (although smaller), and the same bitter taste, as neem (*Azadirachta indica*). In Malaysia it is known as "hempedu bumi" which literally means "bile of earth" since it is one of the most bitter plants used in traditional medicine.³



In traditional Chinese medicine (TCM) it is known as chuan xin lian and is seen as a “cooling, drying” herb used to rid the body of heat, fever and acute infections, and to dispel toxins (heat) from the body especially in disorders of the lungs, throat, urinary system and skin. ‘Heat’ patterns in Chinese medicine involve active inflammation, infection, swelling and, often, burning pain. Examples in which andrographis shows most benefit include raw sore throats, influenza, bronchitis, lung infections and fever. Andrographis has been used traditionally for malaria and early uses as a substitute for quinine have been supported by recent preclinical research. Externally, andrographis is used in TCM to treat oozing wounds, sores, boils, burns and eczema.⁴

Based on its traditional use, andrographis has gained popularity in Western countries in recent years as a treatment for upper respiratory tract infections and influenza. There are reports that andrographis was considered highly efficacious in inhibiting the spread of the influenza epidemic of 1919 in India.^{5,6}

Andrographis is traditionally given as a restorative and tonic in convalescence and used as a choleric to stimulate bile production and flow, which increases appetite and strengthens digestion. It is often used in combination with aromatic herbs, such as peppermint, for stronger digestive effects and to prevent gastrointestinal discomfort at higher doses. It has also been used for protection against the effects of snakebite in some Asian traditions. In India it has been traditionally used for dysentery, cholera, diabetes, tuberculosis, influenza, bronchitis and gonorrhoea. It was also used in the management of many more complex conditions including diabetes, hepatitis and general debility.⁷

Constituents

Bitter diterpenoid lactones (andrographolides), diterpene glucosides, flavonoids, diterpene dimers, xanthones.^{8,9}

Actions

Immune modulator, immunostimulant, bitter tonic, antiviral, antimicrobial, anti-inflammatory, antioxidant, antipyretic, choleric, hepatoprotective, possible adaptogen.

Pharmacological Activity

Immune Modulating Activity

There is reasonably strong evidence from clinical trials to suggest that doses of up to 6g per day of andrographis are effective in decreasing the duration and severity of symptoms (such as sore throat and nasal congestion) of upper respiratory tract infection, in both children and adults, when treatment is started within the first 36 to 48 hours of the onset of symptoms. There is further evidence indicating a protective effect against infection. It has also been studied in human clinical trials for various end-stage cancers (in combination with six other nutraceutical products), HIV infection (using oral andrographolides) and familial Mediterranean fever (with a standardised combination of andrographis, Siberian ginseng (*Eleutherococcus senticosus*), schizandra (*Schisandra chinensis*) and liquorice (*Glycyrrhiza glabra*).^{10,11,12,13}

A recent systematic review (classed as the strongest evidence) of andrographis said it appears to be beneficial and safe for relieving symptoms of acute respiratory tract infections and shortening symptom duration. Thirty-three randomised controlled trials (7175 patients) were included. Andrographis improved cough and sore throat when compared with placebo. It (alone or plus usual care) has a statistically significant effect in improving overall symptoms of acute respiratory tract infections when compared to placebo, usual care and other herbal therapies. Evidence also suggested that it (alone or plus usual care) shortened the duration of cough, sore throat and sick leave/time when compared with usual care. The authors commented that more well-designed trials are needed.¹⁴

A systematic review of seven clinical trials concluded that evidence for the effectiveness of andrographis in the treatment of upper respiratory tract infections is encouraging. The authors commented that one of the challenges about drawing definite conclusions about andrographis is that the majority of the studies have been performed by authors working in collaboration with the leading manufacturer of a standardised andrographis preparation. “It would be helpful if more independent studies were available without

support or involvement of the manufacturer," they said.¹⁵

Two systematic reviews examined the literature on andrographis for upper respiratory tract infection. One found seven double-blind controlled trials of sufficient quality for inclusion. The authors concluded that andrographis appears to be superior to placebo for the treatment of upper respiratory tract infection symptoms. Another systematic review found significant evidence that andrographis is superior to placebo in reducing upper respiratory tract infection symptom severity.^{16,17}

A randomised, double-blind, placebo-controlled clinical study revealed that andrographis was effective in reducing symptoms of upper respiratory tract infection. Symptoms of cough, expectoration, nasal discharge, headache, fever, sore throat, earache, malaise/fatigue and sleep disturbance were scored. A total of 223 patients received either andrographis (200mg/day) or placebo. From days three to five most of the symptoms in the placebo treated group either remained unchanged (cough, headache and earache) or got aggravated (sore throat and sleep disturbance) whereas in the andrographis treated group all symptoms showed a decreasing trend.¹⁸

Results from two randomised controlled trials researching andrographis in mild COVID-19 are expected in mid-2022. One trial in Thailand has more than 3,000 participants comparing andrographis with "standard care" in people with asymptomatic COVID-19. The main outcome the researchers are investigating is how many people in each group end up in hospital within 28 days of a positive COVID-19 test.¹⁹

A small trial in Georgia is testing a combination of andrographis and Siberian ginseng (*Eleutherococcus senticosus*) extract for treating mild COVID-19 symptoms. The standardised combination is known as Kan Jang and has been used for more than 20 years in Scandinavia as a herbal medicinal product in uncomplicated upper respiratory tract infections. Clinical studies confirm that treatment with andrographis either by itself, or in combination with Siberian ginseng (as in Kan Jang), is beneficial in cases of uncomplicated acute upper respiratory tract infections including sinusitis, providing some symptom relief within several days.^{20,21}

Constituents in andrographis with antiviral, antibacterial and anti-inflammatory activity were studied and researchers concluded they could effectively interact with targets of COVID-19 therefore herbal medicines containing these compounds as major components might be meaningful for the treatment of COVID-19 infections however more evidence is needed.²²

Antimicrobial and Antiviral Activity

Andrographis and its metabolites have long been used to treat infectious diseases. A 2021 updated review of andrographis concluded that because it is a promising source of antimicrobial agents, and a safe treatment for infectious diseases, further research is warranted. The review was investigating the potential of andrographis as an antimicrobial agent in relation to the fact that infectious disease is one of the most serious threats to human health globally, further aggravated by antimicrobial resistance. Safe and effective alternatives are required to reduce unnecessary antibiotic prescribing.²³

A recent randomised, double-blind, placebo-controlled trial found that patients with mild to moderate ulcerative colitis, who were treated with andrographis (1800mg daily), were more likely to achieve a clinical response and mucosal healing than those receiving placebo. The trial evaluated the efficacy of andrographis in 180 adults with mild-to-moderate ulcerative colitis, most of whom were failing first-line therapy with mesalamine, a medication used to treat inflammatory bowel disease. Two different strengths of andrographis (1200mg and 1800mg) were compared to placebo over eight weeks. By the end of the treatment period a clinical response was achieved in 60% of patients receiving 1800mg of andrographis per day, compared to 45% taking the 1200mg dose and 40% of those taking placebo. The authors concluded that andrographis could serve as an alternative treatment to steroids, immunosuppressives and anti-tumour necrosis factor biologics (drugs for autoimmune inflammatory diseases) in patients who are not responding to mesalamine. There were also trends for the ability of andrographis to induce remission. While the lower dose (1200mg) of andrographis was not effective in this trial, in a previous controlled trial it had similar efficacy to slow-release mesalamine (4500mg per day) after eight weeks.²⁴

Anti-inflammatory and Hepatoprotective Activity

The findings of a prospective randomised placebo-controlled trial involving 60 patients suggest that andrographis could be a useful "natural complement" in the treatment of rheumatoid arthritis. The authors said a larger trial, and a more extended period of treatment, is necessary in order to confirm these results. Treatment with standardised andrographis tablets three times a day for 14 weeks significantly reduced joint tenderness, number of swollen or tender joints and total grade of swollen or tender joints compared to placebo. A reduction in rheumatoid factor immunoglobulin G and component 4 was also observed. Interestingly participants were not permitted to take non-steroidal anti-inflammatory drugs during the study and paracetamol was only used in cases of severe pain.²⁵

Animal and laboratory studies suggest andrographis may have a number of other potential therapeutic uses including as an anti-inflammatory agent and as a treatment for chemically induced liver damage although these claims need to be tested further.²⁶

Some research shows that high dose andrographis (6g daily) works as well as paracetamol after three to seven days of treatment. One hundred and fifty-two adult patients with pharyngotonsillitis were enrolled in the randomised double-blind study to assess the efficacy of andrographis. The patients were randomised to receive either paracetamol or 3g or 6g per day of andrographis for seven days. The efficacy of paracetamol or high dose andrographis was significantly more than that of low dose andrographis at day three in terms of the relief of fever and sore throat.²⁷

Cardiovascular Activity

Andrographis, and its key constituent andrographolide, have been reported to exhibit potential cardiovascular activities. A 2021 review found they both possess therapeutic potential in the management of myocardial injury, which requires further validation in human clinical trials.²⁸

Indications

- Acute and chronic infections including upper respiratory tract infections, such as the common cold and influenza, asthma, chronic obstructive

airways disease, sore throat (especially tonsillitis), hay fever, fever, weakened immunity, general debility, hyperthyroidism associated with viral infection, urinary infections

- Worm infestation
- Cardiovascular disease, type 2 diabetes
- Ulcerative colitis, diarrhoea, loss of appetite, poor liver function, hepatic conditions, flatulence, dyspepsia, intestinal permeability
- Rheumatoid arthritis, fibromyalgia, chronic fatigue syndrome, HIV infection, multiple sclerosis, Lyme disease
- Skin infections, inflammatory skin disorders such as atopic eczema and psoriasis, ulcers

Energetics

Bitter, cold, dry.

Use in Pregnancy

Not recommended. There is insufficient reliable evidence available to determine safety.

Contraindications

Suspend use one week before major surgery. High doses can occasionally lead to gastric discomfort, anorexia and, in extreme cases, vomiting. When prescribing high doses give smaller doses more frequently to mitigate this.²⁹

While andrographis is usually considered safe concentrated (standardised with andrographolides) andrographis products, particularly ones using methanol as a solvent, have had adverse effects reported to the Australian Therapeutic Goods Administration (TGA) such as taste disturbance and anaphylactic/allergic reactions. It should be noted that the TGA advisory committee stated that in the more traditional uses of andrographis the extract is used in lower concentrations and such products have not been implicated in adverse drug reactions. Traditional preparations include dried plant material, infusions, decoctions and tinctures with extract ratios of between 1:1 and 1:6.

The TGA report said that modern preparations often present the dried andrographis herb in capsule or tablet form, or contain a standardised

extract containing 11.2mg of andrographolides per 200mg of extract, with a typical dose being 400mg thrice daily. The advisory committee said commercial preparations in current use tend to be highly concentrated and standardised extracts, which may significantly change the safety profile of this ingredient. Andrographis preparations with high concentrations of plant to solvent ratio and/or standardised to contain a certain concentration of andrographolide (which go well beyond traditional use) are also now common in complementary medicines marketed to the general public available from pharmacies, health food shops and supermarkets.

Approximately 100 medicines listed in the Australian Register of Therapeutic Goods (ARTG) contain andrographis. All listed medicines (not those for extemporaneous compounding only) released for supply from 2 May 2020 need to comply with TGA requirements for a statement warning consumers about the risk of anaphylactic/allergic reactions with these medicines. Since mid-2019 the TGA has identified a significant increase in the number of adverse event reports involving andrographis and the development of taste disturbance. Most of these reports have been associated with one particular multi-ingredient product which contains andrographis. The TGA have worked with the product sponsor to implement a label warning for the product involved. However, their investigation of this issue indicates that andrographis is likely to be responsible for these effects on the sense of taste.

According to the TGA practitioners should warn clients at the time of purchase of the possibility that products containing andrographis may be associated with changes in the sense of taste (also known as taste disturbance), including complete loss of taste. "The onset of taste disturbance frequently occurs after about two weeks of use of andrographis products, but may also occur in a shorter timeframe. Based on the reports received by the TGA, it can take up to several weeks after you stop using the product for taste to return to normal. In addition, at the time of reporting, not all individuals had regained a normal sense of taste."

The TGA also warns that sudden onset of loss of taste, or altered taste, may be a symptom of a serious medical condition, including COVID-19.

Anyone experiencing loss of taste should seek assessment by a health professional or call the National Coronavirus Helpline on 1800 020 080. If anyone develops any of the following symptoms while taking a product containing andrographis they should stop taking the product as soon as possible and seek medical advice:

- loss of taste
- metallic or soapy taste
- altered taste
- loss of appetite

If a patient who is being treated has presented complaining of reduced or altered taste, or loss of taste functions of the tongue, it should be considered whether a product containing andrographis could be involved. Any concerns or questions about these issues should be discussed with a health professional. If an adverse effect to a product containing andrographis is suspected it should be reported to the TGA.^{30,31,32}

Drug Interactions

Clinical significance of use in combination with immunosuppressive drugs is not clear (theoretical risk) but caution is advised. There is a theoretical risk of increased bleeding with antiplatelet or anticoagulant drugs. The combination may be beneficial with 5-aminosalicylates (e.g. mesalamine, sulphasalazine used to treat inflammatory bowel disease, including ulcerative colitis and Crohn's disease) and anti-rheumatoid arthritis agents (e.g. prednisone, methotrexate) due to possible additive effects. Medical supervision is recommended and caution is advised until more safety data becomes available.³³

Administration and Dosage

Liquid Extract: 1:1

Alcohol: 45%

Weekly Dosage:³⁴ 10 to 20mL

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